JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

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ROY BIRD COOK.

Mr. Cook was born in Weston, W. Va., April 1, 1886, the son of David Bird and Dora Elizabeth Cook. He graduated from the Weston High School in 1904 and became a registered pharmacist in 1905. He was a member of the firm of Ralston and Cook, 1907–1910; and of the Keller-Cook Co., Huntington, W. Va., 1910–1919; from 1919 to 1926 he was connected with Krieg, Wallace and McQuaide Drug Co. in Charleston; and has been president of the Older-Cook Drug Co. since 1926.

Mr. Cook has taken an active interest in Pharmacy since his registration and has served in many capacities in the West Virginia Pharmaceutical Association of which he was a President in 1918–1919. He became a member of the AMERICAN PHARMACEUTICAL ASSOCIATION in 1924 and was chairman of its House of Delegates in 1935–1936. He has been a member of the West Virginia Board of Pharmacy since 1925 and has served as its secretary since 1931. During this period he has been active in the N. A. B. P. of which he is the present president.

Mr. Cook's father was editor of the "Weston Independent" and through this connection the son has been interested in publishing. He is president of the Independent Publishing Co., was associate editor of the West Virginia Review 1925–1936 and was vice-president of the West Virginia Newspaper Council in 1938–1939.

In addition to his interests in Pharmacy and in publishing, Mr. Cook is widely and favorably known as an historian and writer. He is the author of the "Family and Early Life of Stonewall Jackson;" "Lewis County (W. Va.) in the Civil War;" "Washington's Western Lands;" "Annals of Fort Lee;" "Lewis County Journalists and Journalism;" and numerous brochures such as "Rise of Organized Pharmacy in West Virginia," and historical serials. In this connection he has served as a member of the Commission on Historical and Scenic Markers of West Virginia, and of the George Washington Commission, City of Charleston, etc.

Mr. Cook has a number of hobbies but the most important are: A collection of Virginianna and one of the best collections of material on Stonewall Jackson in existence.

In 1907 Mr. Cook and Miss Nelle Williams Camden, daughter of the late John S. Camden of Parkersburg, were married and they have three children: Betty Keith, Eleanor Bird and Mary Randolph (Mrs. Paul Davidson).

Mr. Cook takes an active interest in the civic affairs of Charleston and of the state and is a member of a number of organizations. He has served as president of the Kiwanis Club.

An unusual honor was paid to Mr. Cook in 1937 when the West Virginia University conferred an Honorary Degree of Doctor of Laws (LL.D.) on him in recognition of his contributions in the field of American History and of his services in the field of Pharmacy. In both of these fields and in the many other activities in which he has been interested Mr. Cook has brought credit to his profession.

CALL FOR THE CONVENTION FOR THE REVISION OF THE PHARMACOPOEIA OF THE UNITED STATES OF AMERICA TO BE HELD AT WASHINGTON, D. C., BEGINNING MAY 14, 1940

May 1, 1939

In compliance with the provisions of the Constitution and By-Laws of the United States Pharmacopœial Convention, I hereby invite the several bodies entitled under the Constitution to representation therein to appoint three delegates and three alternates to the Convention for the Revision of the Pharmacopœia of the United States of America, which is to meet in Washington, D. C., on May 14, 1940.

WALTER A. BASTEDO, M.D.,

President of the United States Pharmacopœial Convention.

THE FEDERAL FOOD, DRUG AND COSMETIC ACT.

H. R. 5762 was recently passed by the House of Representatives and has since been passed by the Senate with an amendment referred to later. The purpose of this bill was to postpone the effective date of certain provisions of the Federal Act from June 25, 1939 to January 1, 1940. These provisions require the certification of coal-tar colors used in foods, drugs or cosmetics and that certain affirmative information be given in the labeling of these products. It also proposed to use the terms "name and quantity or proportion" for the terms "name, quantity and percentage" in stating the content of narcotic and hypnotic ingredients on the label of a drug. It was also provided that the effective date with respect to certain labeling might be postponed beyond January 1, 1940, but not further than July 1, in cases where compliance would be unduly costly, with consideration to the public welfare.

The Pepper amendment is: "Provided—That persons who not later than December 1, 1939, notify the secretary by affidavit, setting forth the facts, that compliance on January 1, 1940, with the labeling provisions enumerated in this subsection would be unduly burdensome and that the public interest is being adequately served, shall, as a matter of right, be exempted from compliance therewith until July 1, 1940."

The House declined to accept the Pepper amendment and the bills have gone to conference. No action had been taken at the time this statement was written.

EDITORIAL

E. G. EBERLE, EDITOR EMERITUS. 2215 Constitution Ave., WASHINGTON, D. C.

THE EXCISE TAX ON DISTILLED SPIRITS.—H. R. 6068.

DURING the last annual meetings of the AMERICAN PHARMACEUTICAL ASSOCIATION and the National Association of Retail Druggists, similar resolutions were adopted urging "the Federal and state governments to remove any excise tax from ethyl alcohol used in bona fide medicinal substances with such safeguards and penalties against abuse as may be necessary, in order that the cost of these to the sick may be more reasonable." Other organizations have since endorsed the proposal.

In the December, 1938, issue of the JOURNAL, reference was made to a hearing before the Undersecretary of the Treasury, John N. Hanes, in Washington, on November 10th.

Although it does not propose to eliminate the tax, it is encouraging to report that Mr. Knutson of Minnesota introduced into the House of Representatives, on May 1, 1939, the following bill, H. R. 6068, which was referred to the Committee on Ways and Means of which he is a member:

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled, That section 710 of the Revenue Act of 1938 (relating to the tax on distilled spirits) is amended by adding at the end thereof the following new subsection:

"(*f*) Provided, That upon all ethyl alcohol withdrawn and used for other than beverage purposes, the tax shall be $1.10 per proof gallon."—E. F. K.

INTERNATIONAL CONGRESS OF MILITARY MEDICINE AND PHARMACY.

THE TENTH CONGRESS and the first one to be held in the United States was convened in Washington, D. C., on May 7th and met there until May 15th, with a number of trips to places of interest. The sessions of the Congress were then transferred to New York where they were completed on May 19th with an official banquet. Surgeon General C. R. Reynolds, U. S. Army, served as president of the Congress.

In addition to the general business of the Congress which meets each two years, and a number of Scientific Programs, the following seven questions will be considered at separate meetings; the Organization and Function of the Medical Services in Colonial Expeditions; Probable Casualties in War and Methods of Calculation; Practical Procedures in Anesthesia and Analgesia in War Surgery; Organization and Function of the Military Chemico-Pharmaceutical Service; Emergency Treatment and Primary Apparatus for Fractures of the Jaws in War; Technical Specialization of Administrative Officers in the Medical Service; Oxygen Therapy and Its Practical Use with Troops on Active Duty.

The delegates will spend some time in sight-seeing, attending various social functions and in visiting the many medical facilities in and around Washington.

A number of delegates representing Pharmacy and Pharmaceutical Chemistry will attend and it is encouraging that Pharmacy has been given greater recognition in the Medical Department of the Army in advance of this important International Congress.

Dr. E. N. Gathercoal, former president of the ASSOCIATION, served as an honorary vice-president of the Congress.—E. F. K.

HOW MANY PRESCRIPTIONS TO A PATIENT?

EVERY PHARMACIST should be interested in the answer, but the answer cannot be forthcoming unless you help make it possible. Will you, therefore, as a retail pharmacist, do this for your own benefit as well as for retail Pharmacy in general? Please assign some one to the compiling of the following very simple record (which record when sent in will be combined with others from all states of the union for a national summary).

(1) The total number of new prescriptions compounded during June 1939. (2) How many patients presented one new prescription for compounding? (3) How many customers presented two new prescriptions for compounding? (4) How many customers presented more than two new prescriptions for compounding?

This report should clearly indicate the city and state in which it was made and must be signed. The identity of the store will be kept secret.

Will you also please make a second report which will help answer the question, "Is the Nature of Prescriptions Changing?" This second report can be made at the same time the first report is being compiled. It should be arranged in four parts, each part headed with one of the following captions:

(1) One ingredient prescriptions—nonproprietary; (2) One ingredient prescriptions—proprietary (a brand or trade name product); (3) Several ingredient prescriptions—nonproprietary; (4) Several ingredient prescriptions—proprietary; (5) Several ingredient prescriptions—mixture.

These reports, coming from several cities in each state, should provide an excellent sampling of the national practice which, if it is not now the local practice, will soon become such. Each pharmacist should therefore be interested in the answer to the questions asked.

The month of June has been selected for two reasons. *First*, the reports will be made under like conditions, and *second*, will if mailed in immediately at the close of the month allow enough time for summarization into a report that can be presented at the annual convention next August in Atlanta.

Don't leave this very simple task "to some other pharmacist." It is your chance to help Pharmacy as well as yourself. Don't miss it.

These reports should be addressed to Prof. J. H. Goodness, Massachusetts College of Pharmacy, Boston, Mass. Should you wish, a penny postcard addressed to Professor Goodness will bring you mimeograph sheets with columns arranged to record the information for both reports.—E. F. K.

Papers to be submitted at the Atlanta meeting should be forwarded to the Secretary of the appropriate Section.

REFERENCE STANDARD AND ASSAY FOR THIAMIN CHLORIDE OR VITAMIN B_1.

The Sub-Committee on Scope in 1932 recommended the admission of Dried Yeast to the U. S. P. XI provided a suitable biological assay method could be provided for the standardization of its anti-pellagra activity. The U. S. P. Vitamin Advisory Board immediately undertook this study but were unable to offer such a test and yeast was not admitted to the new Pharmacopœia.

In the meanwhile, however, the vitamin B_1 factor of the vitamin B complex in yeast became increasingly important and the Vitamin Board was asked by the American Medical Association and by manufacturers to provide a Reference Standard for vitamin B_1 and also an assay method which could be endorsed by the Board.

In the initial study which required more than a year and involved many biological assays and a comparison of rat-growth, rat-maintenance, rat-curative and pigeon-curative methods as proposed by various authorities and with the coöperation of about twenty-five laboratories, the Vitamin Board decided upon the restriction of further studies to the rat-curative method. In the meanwhile the U. S. P. Board of Trustees, with the help of the Vitamin Board had provided a U. S. P. Reference Standard for vitamin B_1 for use in this country.

This U. S. P. Standard was identical with the International adsorbate standard and was prepared and standardized by Dr. C. P. Jansen of Amsterdam.

By this time crystalline vitamin B_1 had been synthesized by Dr. R. R. Williams and it became apparent that this definite chemical substance would ultimately replace the adsorbate as the vitamin B_1 standard. The Vitamin Board therefore immediately added to its investigation the potency of pure synthetic crystalline vitamin B_1 in terms of International Units and the same group of laboratories undertook the comparison of four suggested rat-curative assay methods. At the same time the comparative potency of the International standard and the crystalline material was determined. The Board of Trustees authorized the procuring of a considerable quantity of the synthetic crystalline vitamin B_1 from two independent sources and this was mixed, dissolved, recrystallized and packaged.

In the subsequent biologic tests by sixteen laboratories the majority of workers and also the U. S. P. Board decided upon the adoption for Pharmacopœial purposes of one of the methods being tried and also determined that the potency of the crystalline vitamin B_1, prepared for use as the new U. S. P. Reference Standard, was equivalent to 333 units in each mg. corresponding to 3 micrograms (3γ) = 1 International or U. S. P. Unit.

At approximately the same date the Biological Committee of the Health Organization of the League of Nations, who had been making similar tests announced the same value for the new International vitamin B_1 standard.

The following announcement was made by the League of Nations Committee.

"The International Conference on Vitamin Standardization, at its 1934 meeting, recommended that the potency of the existing vitamin B_1 standard, the standard adsorption product, 'should be tested relatively to that of the crystalline vitamin B_1 preparations then available with the aim of ultimately adopting pure crystalline vitamin B_1 as international standard.' During the past two years, this possibility has been brought nearer by the discovery, almost simultaneously in three different countries of methods for production of the pure vitamin by synthetic processes.

"Through the good offices of Sir Henry Dale, 70 Gm. of synthetic vitamin B_1 hydrochloride were generously provided by the following four firms: Messrs. Merck and Company, Rahway, N. J.; Messrs. E. Merck, Darmstadt; Messrs. F. Hoffmann-La Roche, Basle; and Messrs. I. G. Farbenindustrie, Elberfeld. The samples were mixed and the whole recrystallized by Dr. A. R. Todd at the Lister Institute. The final sample, 55 Gm., gave satisfactory criteria for purity as follows:

"*Vitamin B_1 (aneurin) hydrochloride:* Colorless monoclinic plates m. p. 246–247° (de comp.). *Picrate:* Yellow needles, m. p. 208° (decomp.). *Picrolonate:* Dimorphous, (*a*) Yellow needles, m. p. 165° (decomp.). (*b*) Yellow prisms, m. p. 226° (decomp.).

"Specimens of this material and of the present acid clay standard were distributed from the National Institute for Medical Research to twenty-two laboratories for examination and biological and chemical determination of the potency of the crystalline vitamin in terms of the present standard. Seventeen reports have been received, comprising thirty-one separate comparative experiments."

The new U. S. P. crystalline vitamin B_1 Reference Standard therefore is available now for research or for use in the standardization of vitamin B_1 preparations and may be obtained through the office of the Chairman of the Committee of Revision, at 43rd and Woodland Ave., Philadelphia, Pa.

The following instruction for use has been provided by the Vitamin Advisory Board.

SUGGESTIONS FOR USING THE U. S. P. REFERENCE STANDARD FOR VITAMIN B_1 (THIAMIN CHLORIDE).

Before preparing a solution dry the standard crystalline vitamin B_1 to constant weight in a desiccator over phosphorous pentoxide.

Precautions to Be Taken in the Preparation of Solutions.—The pure vitamin B_1 hydrochloride, if completely desiccated by exposure to vacuum at a high temperature, is very hygroscopic. In the form adopted for the standard preparation, containing approximately 1 molecule of water of crystallization, it is much less hygroscopic, but still gains weight if exposed to ordinary, moist air. It is preferable, therefore, to transfer the quantity required for a test to a small glass-stoppered weighing bottle, in which it can then be weighed on a microbalance, or an ordinary balance, according to the number of tests for which the sample is being taken. Even without such precautions, however, exposure to the air during weighing will not cause an increase in weight of more than about 0.6 per cent, if the operations are completed within five minutes.

Neutral and alkaline solutions of the standard are unstable, and aqueous acid solutions are readily infected by molds, which inactivate the vitamin. It is recommended, therefore, that stock solutions ($^1/_2$ mg. per cc. is a convenient strength) should be prepared in 25 per cent, aqueous ethyl alcohol to which hydrochloric acid is added to make the solution approximately $N/500$ HCl. This solution is stable if kept at about 4° C. Solutions of suitable strength for animal dosage (20 to 100 micrograms per cc.) must be made at least twice weekly from the stock solution by dilution with distilled water. Such dilutions must be kept at a low temperature and examined daily for molds.

The details of the bio-assay method proposed for inclusion in the Second U. S. P. XI Supplement are as follows:

BIO-ASSAY FOR DETERMINING THE POTENCY OF VITAMIN B_1.

Method of Assay for Thiamin Chloride (Vitamin B_1).

The assay of U. S. P. products for vitamin B_1 potency shall be by comparison with the U. S. P. vitamin B_1 Reference Standard, by assay procedure conforming in all respects to the following specifications:

The vitamin B_1 assay, comprising the recording of observations of rats throughout specified periods of their lives while being maintained on specified dietary regimens and the interpretation of such data, is as follows:

Preliminary Period.—Throughout the preliminary period each rat shall be raised under the immediate supervision of, or according to directions specified by, the assayer. Throughout the preliminary period the rats shall be maintained on a dietary regimen which shall provide for normal development in all respects, except that the vitamin B_1 intake may be restricted.

Depletion Period.—A rat shall be suitable for the depletion period when the age of the rat does not exceed thirty (30) days, and if the body weight of the rat does not exceed 50 Gm. and if the animal manifests no evidence of injury or disease or anatomical abnormality which might hinder growth and development. Throughout the depletion period each rat shall be provided with the vitamin B_1 test diet and water (U. S. P.) ad libitum, and during this period no other dietary supplement shall be available to the animal. Throughout the depletion period and until the assay shall have been completed the rats shall be kept in cages provided with a wire cloth bottom, each mesh of which shall be not less than $^1/_2$ inch.

Assay Period.—A rat shall be suitable for the assay period provided that the depletion period shall not have exceeded 75 days, and provided that the rat shall manifest evidence of vitamin B_1 deficiency characterized by acute polyneuritis. Throughout the assay period each rat shall be kept in an individual cage and provided with the vitamin B_1 test diet compounded from the same lots of ingredients, and water (U. S. P.) ad libitum. On the day beginning the assay period there

shall be administered to each rat a single dose of the reference standard of such size that it will produce in individual animals a curative period of not less than 5 days and not more than 15 days. All of the rats used in any one assay shall receive the same quantity of the reference standard. Each rat shall then be observed for the cure of and recurrence of polyneuritis, and when polyneuritis reaches the same acute stage observed when the reference standard was administered, a single dose of the assay product shall be administered. The animals shall then be observed to determine if polyneuritis is cured, and if so, observation shall be made of the duration of the period. Each assay shall include successive administrations of the reference standard and assay product to not less than eight rats. The assay product may be administered orally or parenterally but in any one assay the reference standard shall be administered in the same manner as the assay product, and the quantity of the assay product administered to each rat shall be the same.

Recording of Data.—On the day beginning the depletion period and at intervals of not more than seven (7) days during the depletion period, a record shall be made of the body weight of each rat. On about the twenty-fifth (25) day and each day thereafter for the remainder of the depletion period, each rat shall be observed for symptoms of polyneuritis. The following dates shall be recorded:

1. The day on which the reference standard is administered.
2. The day on which cure of polyneuritis is observed following the administration of the reference standard.
3. The day on which acute polyneuritis recurs and the assay product is fed.
4. The day on which cure of polyneuritis is observed following the administration of the assay product.
5. The day on which acute polyneuritis recurs after the administration of the assay product.

Vitamin B_1 Potency of the Assay Product.—In determining the vitamin B_1 potency of the assay product the duration of the curative period following the administration of the reference standard and the assay product shall be considered. The dose of assay product administered contains an amount of vitamin B_1 equal to or greater than that contained in the dose of the reference standard administered if that quantity promotes in the assay animals a total curative period (the sum of the number of days of the curative period of each of the animals) equal to or greater than the total curative period produced by administration of the reference standard.

Definitions.—As used herein, unless the context otherwise indicates the term "acute polyneuritis" means that stage of vitamin B_1 deficiency in which the animal regains control of the voluntary muscles, as evidenced by standing or walking, a few seconds after extreme muscular contraction, which has been induced by twirling the rat by its tail. (Onset of acute polyneuritis is invariably accompanied by loss in body weight); the term "assay period" means the interval in the life of a rat between the last day of the depletion period and the final observation following the administration of the assay product; the term "assay product" means a product under examination for its vitamin B_1 potency; the term "curative period" is the interval of time between the administration of vitamin B_1 and the subsequent recurrence of acute polyneuritis after a complete disappearance of polyneuritic symptoms, and the duration of the curative period is expressed as the number of days in that interval; the term "cure of polyneuritis" means the complete disappearance of polyneuritic symptoms and is invariably accompanied by increase in body weight; the term "depletion period" means the interval in the life of a rat during which its food intake is only the vitamin B_1 test diet and water (U. S. P.); the term "preliminary period" means the interval in the life of a rat prior to the depletion period; the term "reference standard" means the U. S. P. vitamin B_1 reference standard, distributed by the Board of Trustees of the U. S. Pharmacopœial Convention, and which contains one U. S. P. unit of vitamin B_1 in each 3 micrograms; the term "vitamin B_1 test diet" means a uniform mixture which has not been compounded for more than seven (7) days of the following food materials and in the proportions designated:

VITAMIN B_1 TEST DIET.

Sucrose	60.25 per cent
Casein (1)	18.00 per cent
Salt mixture (2)	4.00 per cent

Autoclaved yeast (3)	5.00 per cent
Autoclaved peanuts (4)	10.00 per cent
Purified liver extract (5)	0.75 per cent
Cod liver oil (U. S. P.)	2.00 per cent

(1) The casein shall be free from demonstrable traces of vitamin B_1.

(2) The salt mixture shall be either salt mixture No. 1, described on page 479,* or a salt mixture having essentially the same proportions of the elements.

(3) Dried yeast which has been autoclaved in steam at 15 pounds pressure for 5 hours with the yeast spread in a layer not more than $^1/_4$ inch in depth and then dried at a temperature not exceeding 65° C.

(4) Unroasted shelled No. 1 grade Virginia peanuts are crushed in a food chopper, autoclaved in steam at 15 pounds pressure for 5 hours with the ground peanuts spread in a layer not more than $^1/_2$ inch in depth, and then dried at a temperature not exceeding 65° C. This preparation may be incorporated in the basal diet by grinding with the requisite quantity of sucrose.

(5) One hundred grams of Extract of Liver, U. S. P., are dissolved in 200 cc. of water. One thousand cubic centimeters of 95 per cent ethyl alcohol, followed by 1200 cc. of ethyl ether, are added with constant stirring. After precipitation is complete (usually five to fifteen minutes) the material is filtered through paper, reasonable care being taken to prevent loss of ether. The residue is redissolved in 200 cc. of water and precipitation and filtration are repeated as above. The solution of the residue and precipitation is repeated a third time. The final residue, after drying at a temperature not exceeding 65° C., constitutes the purified liver extract. Drying may be facilitated by evaporating a water solution of the final residue on a small quantity of vitamin B_1-free casein. One hundred grams of Extract of Liver, U. S. P., will yield approximately 75 Gm. of purified liver extract.

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It is further expected that synthetic crystalline vitamin B_1, under the title Thiamin Chloride will become official in the Second U. S. P. XI Supplement but no bio-assay will be required for the pure chemical since the physical and chemical tests available will adequately control its quality and if it meets these specifications it is believed that its therapeutic activity will be uniform.

E. FULLERTON COOK,
Chairman of the Committee of Revision of the U. S. Pharmacopœia.

Released April 17, 1939.

AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE. PROGRAM OF PHARMACY SUB-SECTION N-2 OF THE MEDICAL SCIENCES SECTION.

A SYMPOSIUM ON THE VITAMINS WITH PARTICULAR REFERENCE TO THEIR STANDARDIZATION.

Tuesday, June 20th, 10:00 A.M. (first session).

The Vitamin B Complex

1. Vitamin B_1, Thiamin, by Aaron Arnold, Ph.D. (30 minutes).
2. Riboflavin, by P. H. Phillips, Ph.D.(30 minutes).
3. Nicotinic Acid, by C. A. Elvehjem, Ph.D. (30 minutes).

Tuesday, June 20th, 2:00 P.M.

4. Chick Antidermatitis Factor and Vitamin B_6, by W. D. Woolley, Ph.D. (30 minutes).
5. Vitamin A, by A. Black, Ph.D. (30 minutes).
6. Vitamin E, Mrs. F. P. Dann (30 minutes).

GLENN L. JENKINS, *Chairman Program Committee.*

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* U. S. P. XI.

SECTIONS

BOARD OF REVIEW OF PAPERS (SCIENTIFIC SECTION).—*Chairman*, F. E. Bibbins; H. M. Burlage, W. G. Crockett, E. V. Lynn, C. O. Lee, L. W. Rising, L. W. Rowe, Heber W. Youngken, Ralph E. Terry, Carl J. Klemme.

CAFFEINE EFFECTS UPON THE ACTIVITY OF THE LONGITUDINAL MUSCLES OF THE SMALL INTESTINE.[1]

BY RALPH H. CHENEY.[2]

An extensive literature has dealt with the effect of various substances upon the spontaneous activity and upon the normal physiological state of the small intestine. Prior to 1916, many investigators aided in the development of methods and reported generalities which made possible the more detailed studies with reference to specific effects upon the several levels of the gut and upon the longitudinal and circular musculature separately. A series of illuminating studies which have significance to the present study, began about 1916 by Salant and Mitchell ('16) on the heavy metals, Salant and Schwartze ('17) on sodium citrate, Taylor and Alvarez ('17) on temperature effects, Alvarez ('18a) on differences in the behavior of different levels of the intestine, Alvarez (18b) on the effects of drug action upon intestinal rhythmicity and Kruse ('19–'20) on the action of bromide.

Since 1920, the effects of a greater variety of substances upon the intestine and upon smooth muscle generally have been reported. Müller ('21) published a series of photomicrograms to illustrate the nerves of the intestinal wall. Frédericq and Mélon ('23) reported the caffeine-adrenalin antagonism with reference to intestinal motility. The isolated duodenal segments of the rabbit were used as the experimental material. King and Arnold ('22) discussed the activities of the intestinal mucosal motor mechanism. They concluded that the intestinal mucosa stimulation was a local reaction and myogenetic in origin. The rôle of a change in p_H in the regulation and control of the motor activities of the small intestine was emphasized by Hammett ('22). Evans and Underhill ('23) also dealt with p_H effects on the tonus and contractions of smooth muscle. Gross and Clark ('23) reported the influence of the oxygen supply on the response of the isolated intestine to drugs. The work of Henderson ('23) on atropin effects, Roth ('23) on barium chloride action, Crane and Henderson ('24) on the sensitivity to internal pressure, the extensive study by La Barre ('24) on opium alkaloids, by Tiegs ('24, '25) on the nerve net and its relation to the automatic rhythmic movements of plain muscle in the frog's stomach, by Burnett ('25) on variations in the intestinal rate, and the reports by Rademaekers and Sollmann ('24) added considerable specific data to the general problem of the pharmacology of the intestine.

Between 1925 and 1930, informative contributions were made by D'Haenens ('25) on eserine and atropin, by Alvarez ('25) on the slow tonus rhythm in the bowel, by De Boer, Dreyer and Clark ('25) on the several constituents of the body

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[1] From the laboratories of the Brooklyn College of Pharmacy, L. I. University, Brooklyn, New York, and the Marine Biological Laboratory, Woods Hole, Mass.

[2] Professor of Biology, Long Island University.

fluids which act as plain muscle stimulants, by Gruber ('26) reporting that narcotics cause a loss of tonus of excised strips of plain muscle, by Polansky ('27) on yeast extract effects, by Sollmann ('27) on the effect of mechanical and physical conditions upon the response of the rabbit's ileum, by whitehead ('29) on the responses of the excised rabbit intestine to alterations of electrolytic concentrations, by von Oettingen ('29) on the simultaneous cinematography of intestinal movements and tracings, by Frédericq ('30) on chronaxie, and by Waucomont ('30) in an extensive article on the general pharmacology of the intestine of the rabbit and dog.

Since 1930, many articles have dealt with the pharmacology and physiology of smooth muscle and of the intestine in particular. Papers of special importance during this period with reference to the current report have been published by Komant ('32) dealing with the stimulating action of caffeine, theobromine and theophylline, by Salant and Parkins ('32) on ergotamine and ion influences, by Rabbeno and Cisbani ('32) on the digestive tube pharmacology in the frog, by Epstein ('33) on the response of the alimentary tract to autonomic drugs, by Hockett, Newman and Thienes ('33) on the reciprocal activity of the muscular coats of the guinea pig, by Hoyt, Patek and Thienes ('34) with the beginning of a series of articles on smooth muscle action, and by Emerson ('36) on the biochemical effect of ether on the gut. In 1937, a number of valuable contributions included a paper by Van Liere and Emerson ('37) on the absorption of digitalis from the small intestine during anoxemia, and one by Reynolds ('37) on smooth muscle action in a study of the control of uterine contractility. A preliminary statement was made by Cheney ('37) of my present studies of the caffeine effects upon the myenteric activity in the rabbit.

Donatelli ('38) discussed a new cannula for smooth-muscled tubular organs and described a system for recording the activity of the circular and longitudinal muscles simultaneously with relative ease. Several papers on smooth muscle have been published by Singh ('38) studying the properties of tonic contraction in smooth muscle, by Fischer ('38) on invertebrate smooth muscle birefringence, by Farmer ('38) on the inhibitory action of narcotics on the histamine contraction of the plain musculature of the guinea pig, by McLachlin ('38) on the action of ergometrine on the isolated human uterus, by Lazarus ('38) on the action of urea upon the small intestine of the rabbit, and a particularly significant paper by Beard and Pizzolato ('38) involving the effect of caffeine upon the creatine-creatinine metabolism which is of interest to the explanation of muscle physiology and pharmacology generally. An article by Franklin and Maher-Loughnan ('38) on the circular musculature of the small intestine of the cat throws some light upon the behavior upon the longitudinal muscles. Eichler's ('38) recent volume, "Kaffee und Koffein" primarily reviews the literature from 1920 to 1938 and includes brief data and references to the effects upon the intestine.

With a few exceptions such as the report by Plant and Reynolds ('22) who noted the improvement of peristaltic movements with caffeine, and the more recent paper by Komant in 1932, recent researches have not dealt specifically and in detail with the influence of caffeine upon myenteric activity. The current paper gives evidence of the effect of the purine complex, caffeine, following its absorption through the mucosa, upon the intrinsic muscular motility of the isolated segments

of the small intestine of the rabbit. Individual and comparative sensitivities of three regions of the gut are discussed with reference to the response of their longitudinal musculature during and after caffeine perfusion. The phenomena of rhythmicity, rate, tonus and amplitude are shown for each region studied by means of kymographic records.

GENERAL METHOD.

Animals were sacrified by a blow on the occiput in order to avoid any anesthetic effect. Only actively rhythmic segments were employed because it has been pointed out by Hooker ('12) that rhythmic and arrhythmic segments respond differently to the *same* stimulus. In addition, specifically comparable regions were used: namely, the proximal descending duodenum, the mid jejunum and the proximal ileum. This precaution was necessary in accordance with the study by Magee and Southgate ('28) on salt effects and their demonstration of the fact that considerable difference exists—the degree of sensitivity of the several levels of the gut to the same chemical substance.

A study of various recording methods was made as given by Abderhalden ('29) and especially of the methods employed by Trendelenburg ('13,' 17), by Plant and Reynolds ('22), by Sollmann and Rademaekers ('26), by Salant and Brodman ('29) and by Bernheim ('33). A modification of the Trendelenburg apparatus was chosen for recording the longitudinal contractions on the basis of the required accuracy within the limits of the preparation used, practicability, definiteness and reproducibility of experimental results. It was essentially the modification employed by Polansky ('27) but arranged for the recording of the longitudinal musculature only.

The common rabbit (Lepus) was used. Maintenance of uniform conditions for the perfusion of caffeine through the lumen of the isolated segment was attained with regard to the preparation of the nutrient medium, the experimental medium, pressure, temperature, oxygenation, time intervals, p_H and recording mechanics. These controls of the apparatus and the procedures exercised in the preparation of the experimental material were in accordance with the requirements indicated by the investigations referred to in the literature cited previously.

EXPERIMENTAL PROCEDURE.

1. Non-excited animal sacrificed by a blow on the occiput. (The animal had not been fed for 24 hours but fed a few minutes prior to death.) Desanguinated immediately *via* carotid artery and jugular veins.

2. Following a long anterior-posterior incision along the mid-ventral line, the donor's viscera was exposed and an actively rhythmic segment 6 to 7 cm. long was removed with precision from the desired area. When attached to the apparatus, an actively rhythmic length of 4 cm. was employed uniformly.

3. Segments were handled with precautions not to cause mechanical pinching or other stimulation. Placed in a paraffined petri dish flooded with mammalian Tyrode's solution at 38° C. and buffered to p_H 7.55, the segment was pressed gently from the proximal (or oral) end to the distal (or cæcal) termination to remove any contents of the lumen. Then a pipette caused the warm Tyrode to gently flood the lumen in the same direction thereby washing thoroughly and preventing auto-intoxication.

4. Attachment to perfusion apparatus by flared glass cannulas so that the perfusion would flow in the same (its normal) direction.

5. Adjustment of mechanical, electrical and thermal units for uniform experimental conditions regarding the factors mentioned. The excised segment was allowed to contract rhythmically under approximately natural conditions in a warm bath of oxygenated Tyrode's solution.

6. Recording of longitudinal contraction by means of a bees-waxed, silk thread from the preparation to the writing lever was allowed to proceed until normal behavior was observed in all details.

7. Changes in perfusion fluids could be accomplished at any moment by means of a two-way stop-cock.

DISCUSSION.

Direct excitation of all intestinal smooth muscle by nerves is improbable because there are more muscle cells than there are nerve fibers. The intestine, however, possesses abundant nerve plexuses within its walls. The subserous, myenteric plexus of Auerbach with its network of fibers and cells between the longitudinal and circular muscles and the submucosal plexus of Meissner are well known. Moreover, the ganglion cells of Auerbach's plexus serve as the ganglionic cells for vagus connections and possibly for the sympathetic nervous system. Undoubtedly, the extrinsic plexis is involved normally in the stimulation and control of the intestinal motility and functions as an additional safety factor as suggested by Thomas and Kuntz ('26) and by Henderson ('28). The extrinsic nerve supply, however, can be eliminated and intestinal motility will persist. Alvarez and Mahoney ('22) and Gasser ('26) have shown that smooth muscle even when it is devoid of *all* nervous elements maintains a spontaneous rhythm and tonus.

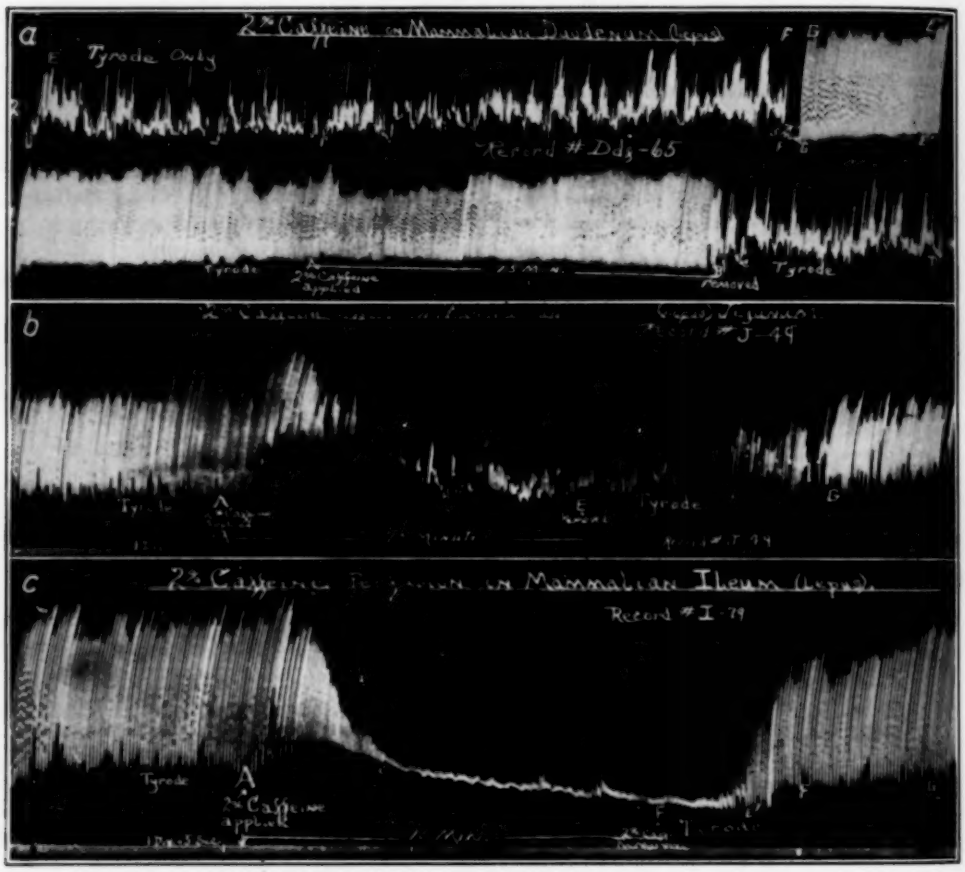

Fig. 1.—Effect of Caffeine (2%) upon the Intrinsic Myogenetic Responses of the Longitudinal Musculature of the Rabbit Intestine. (*a*) Duodenum Record No. Ddf–65. (*b*) Jejunum Record No. J–49. (*c*) Ileum Record No. I–79.

Moreover, Swirski ('02) demonstrated that the excitation of the intestinal motility depends upon fiber to fiber excitation by mechanical distension and upon the *nature* of the lumen contents. It is known that smooth muscle is more susceptible to *chemical* excitation than is skeletal muscle. In view of these facts, my procedure here permits the observation and comparison of the effects of caffeine in different concentrations upon the longitudinal musculature of similar segments. The

perfusion solutions used were as follows: 2%, 1%, 0.5%, 0.1%, 0.05% pure caffeine, alkaloid, U. S. P. Powder (Merck).

As pointed out by Verzár and McDougall ('36) in their monograph, the purines are absorbed normally by the blood vessels as they are not present in the lymph. Obviously, it is apparent that, with the elimination of the circulatory distribution of the caffeine and with the decentralization of nervous control in the preparation which I employed, the contact between the longitudinal musculature and the caffeine was possible only by absorption through the mucosa and subsequent diffusive distribution. It should be noted also that Šiaulis and Sollmann ('26, '27) concluded that the longitudinal and circular muscle layers contract independently; and that, although the contractile force of one muscle layer may stimulate the other to contract, there is no absolutely dependent correlation between the two sets of muscles. Therefore, it is possible to record the action of either set separately with the apparatus and preparation employed under the conditions of the experiments which I am reporting here. It should be appreciated, however, that the observations derived from the excised segment do not preclude the possibility that some neuro-muscular coördination may exist in the intact animal.

The preparation utilized in this study has certain definite limitations with regard to the transfer of the results "in toto" to the intact intestine. It has also the desirable elimination of various complicating factors regarding the observation of direct caffeine effects. It furnishes a favorable intestinal muscle-preparation for the study of modifications in the muscular activity due to the variation of a single chemical complex—in this case, caffeine—in the perfusing fluid. The alterations in the normal behavior of such a segment are a convenient measure of the direct myogenetic effects in response to a given substance.

For the sake of brevity and because of the fact that only the concentrated solutions of caffeine are consistently effective, only the 2% caffeine effects are presented by their kymographic records on each of the three levels of the small intestine. (See Fig. 1.) The responses of comparable segments to the perfusion by other percentages of caffeine are condensed in Table I. The data derived from the *individual* effects of five different percentages of caffeine upon the *same* intestinal area, gives the basis for a comparison of the sensitivities between the *several* areas which were subjected to the same series of caffeine perfusions.

TABLE I.—COMPARATIVE SENSITIVITY OF INTESTINAL AREAS TO CAFFEINE.

Comparative Sensitivity (all factors considered).

Key: 1. First effective; most effective; first recovery.
2. Next in order.
3. Least or last in order.

% Caffeine in Perfusion Solution.	Intestinal Segment.	Order of First Effect.	Degree of Effect.	Order of Recovery.	Final Recovery Complete or Incomplete.
2%	Duodenum	3	3	3	Complete
	Jejunum	2	2	2	Complete
	Ileum	1	1	1	Complete
1%	Duodenum	3	3	1	Complete
	Jejunum	2	2	2	Complete
	Ileum	1	1	3	Complete
0.5%	Duodenum	1	1	2	Complete
	Jejunum	3	2	3	Complete
	Ileum	2	3	1	Complete
0.1%	Duodenum	No effect	...	...	...
	Jejunum	Effective	Slight	Rapid	Complete
	Ileum	No effect	...	...	...
0.05%	Duodenum	No effect	...	...	...
	Jejunum	No effect	...	...	...
	Ileum	No effect	...	...	...

An examination of Fig. 1 reveals the actual variations in the activity of the longitudinal musculature of the rabbit which were produced by perfusing the duodenal, jejunal and ileal segments with 2% caffeine-in-Tyrode solutions.

Record No. Ddf–65 demonstrates the effect upon the duodenum. Normal behavior is recorded from the left end of the lower line up to point "A" when the caffeine perfusion began and was continued for a fifteen minute period. A very slight tonus improvement may be noted which is accompanied by an amplitude decrease. Both effects were corrected at somewhat less than the half-way period of the perfusion. With the removal of the caffeine and the substitution of the normal nutrient Tyrode solution at "B," a delayed caffeine effect began to develop, an improved tonus and reduced amplitude effect rapidly becoming drastic between "B" and "C," persisting through the time interval from "B" to "F" inclusive. Full recovery occurred during the five minute interval from "F" to "G." The recovery occurs more abruptly than the original variations appear in the normal.

Record No. J–49 shows the effect upon the jejunum. With the caffeine applied at "A," an effective variation occurs more promptly than in the duodenum. Moreover, the tonus increase and amplitude decrease do not occur simultaneously. At "B" a drastic tonus improvement occurs suddenly but the amplitude decrease does not appear until the mid-way time interval between "B" and "C." With the development of the drastic amplitude reduction at "C," the tonus level falls rapidly to approximately the normal level and is maintained during the remainder of the perfusion period whereas the amplitude depression persists to point "G" when approximately full recovery occurs. The caffeine effect develops more rapidly in the jejunum than in the duodenum and the recovery time is much less in the jejunum.

Record No. I–79 presents the effect upon the ileum. Following the application of caffeine at "A," an improved tonus and a decreased amplitude develop rapidly in approximately the same time interval as in the jejunum. The tonus improvement is proportionately less than in the jejunum and the amplitude decrease is proportionately more than in the jejunum. With the cessation of the caffeine perfusion and the return of the normal nutrient Tyrode at "E," the drastic variation in the normal behavior persists to "É," when a rapid recovery begins which becomes full recovery between "F" and "G." This complete recovery is appreciably more rapid in the ileum than in the jejunum and much more rapid than in the duodenum.

CONCLUSIONS.

1. The three regions of the mammalian small intestine possess individual and different sensitivities with respect to their intrinsic motility in response to the caffeine stimulation of the longitudinal muscles.

2. Since complete recovery occurs, even after perfusion with 2% caffeine solutions (2.2% would be saturation), in each of the three primary levels of the gut and since the effect of lower percentages is variable, no part of the small intestine can be described as highly sensitive to the action of caffeine.

3. From a study of the kymographic records which were obtained from 150 experiments,[1] it is evident that the degree of tonicity and the amplitude of contraction were affected by caffeine to a greater extent than is indicated by any variation in the rhythmicity or rate, which was negligible. The tendency in all three segments is to improve the tonus and decrease the amplitude temporarily of the longitudinal musculature in each case. It is of interest that caffeine affects the tonicity in view of the fact that the exhibition of tonus when separated from the central nervous system is one of the chief behavioristic differences between smooth and striated muscle. Caffeine affects the smooth muscle of the intestine directly as it is known to do in both striated and cardiac muscle.

4. In accordance with the general observations of Alvarez and Mahoney ('22) that the gastro-intestinal tract shows decreasing gradients from the oral to the anal (cæcal) termination with reference to rhythmicity, frequency of contractions

[1] I take this opportunity to thank my former research assistant, Mr. Isador Shaw, for his careful manipulation of the apparatus and of the preparations throughout these investigations.

and the metabolic rate, it might be presumed that the caffeine effects upon these factors would follow a similar sequence. Such a correlation does not exist. There is no absolute gradient for the time or degree of caffeine effects or for the rate of recovery in the longitudinal musculature of the small intestine. The separate intestinal areas, however, demonstrate a distinct difference in the degree of their sensitivity to a given concentration of caffeine.

5. It is suggestive that the combined effects of caffeine upon the myogenic activity of the longitudinal musculature of the intestine are such that the absorption of caffeine from the lumen may improve the physical factors of pressure and movement. Thereby, the process of the absorption of nutrients from the lumen would be facilitated.

LITERATURE CITED IN CHRONOLOGICAL ORDER.

(1) Swirski, *Naunyn-Schmiedebergs Arch. f. exper. Path. u. Pharmakol.*, 48, 282 (1902).
(2) Hooker, *Am. J. Physiol.*, 31, 47 (1912).
(3) Trendelenburg, *Ztschr. f. Biol.*, 61, 67 (1913).
(4) Salant and Mitchell, *Am. J. Physiol.*, 39, 355 (1916).
(5) Salant and Schwartze, *J. Pharmacol. and Exp. Therap.*, 9, 497 (1917).
(6) Taylor and Alvarez, *Am. J. Physiol.*, 44, 344 (1917).
(7) Trendelenburg, *Naunyn-Schmiedebergs Arch. f. exper. Path. u. Pharmakol.*, 81, 55 (1917).
(8) Alvarez, *Am. J. Physiol.*, 45, 342 (1918*a*).
(9) Alvarez, *Ibid.*, 46, 554 (1918*b*).
(10) Kruse, *J. Pharmacol. and Exp. Therap.*, 14, 149 (1919–1920).
(11) Müller, *Upsala Läkarenf. Forh.*, 26, 1 (1921).
(12) Plant and Reynolds, *Proc. J. Pharmacol. and Exper. Therap.*, 19, 256 (1922).
(13) Alvarez and Mahoney, *Am. J. Physiol.*, 59, 421 (1922).
(14) Frédericq and Mélon, *Compt. rend. Soc. de biol.*, 87, 92 (1922).
(15) King and Arnold, *Am. J. Physiol.* 59, 97 (1922).
(16) Hammett, *Ibid.*, 60, 52 (1922).
(17) Evans and Underhill, *J. Physiol.*, 58, 1 (1923).
(18) Gross and Clark, *Ibid.*, 57, 457 (1923).
(19) Henderson, *Arch. de internat. Pharmacodyn. et de Thérapie*, 27, 205 (1923).
(20) Roth, *Ibid.*, 27, 333 (1923).
(21) Crane and Henderson, *Am. J. Physiol.*, 70, 22 (1924).
(22) La Barre, *Arch. de internat. Pharmacodyn. et de Thérapie*, 29, 179 (1924).
(22a) Rademaekers and Sollmann, *Ibid.*, 29, 481 (1924).
(23) Tiegs, *Australian J. Exper. Biol. and M. Sc.*, 1, 131 (1924).
(24) Tiegs, *Ibid.*, 2, 157 (1925).
(25) Burnett, *J. A. M. A.*, 85, 1777 (1925).
(26) D'Haenens, *Ibid.*, 30, 77 (1925).
(27) Alvarez, *Am. J. Physiol.*, 74 ,181 (1925).
(28) De Boer, Dreyer and Clark, *Arch. de internat. Pharmacodyn. et de Thérapie*, 30, 141 (1925).
(29) Abderhalden, *Handb. biol. Arbeitsmeth., Abt. V, Teil 5A, Heft* 5, 843 (1929).
(30) Sollmann and Rademaekers, *Arch. de internat. Pharmacodyn. et de Thérapie*, 31, 39 (1926).
(31) Thomas and Kuntz, *Am. J. Physiol.*, 76, 606 (1926).
(32) Gasser, *J. Pharmacol. and Exper. Therap.*, 27, 395 (1926).
(33) Šiaulis and Sollmann, *Arch. de internat. Pharmacodyn. et de Thérapie*, 32, 340 (1926).
(34) Gruber, *J. Pharmacol. and Exper. Therap.*, 30, 149 (1926).
(35) Šiaulis and Sollmann, *Am. J. Physiol.*, 81, 579 (1927).
(36) Sollmann, *Ibid.*, 81, 579 (1927).
(37) Polansky, *Ibid.*, 83, 488 (1927–1928).

(38) Henderson, *Am. J. Physiol.*, 86, 82 (1928).
(39) Magee and Southgate, *J. Physiol.*, 65, Proc. VII (1928).
(40) Whitehead, *Am. J. Physiol.*, 89, 253 (1929).
(41) von Oettingen, *Ibid.*, 90, 464 (1929).
(42) Salant and Brodman, *J. Pharmacol. and Exper. Therap.*, 37, 55 (1929).
(43) Frédericq, *Arch. de internat. Pharmacodyn. et de Thérapie*, 38, 438 (1930).
(44) Waucomont, *Ibid.*, 36, 285 (1930).
(45) Komant, *Naunyn-Schmiedeberg's Arch. f. exper. Path. u. Pharmakol.*, 163, 635 (1932).
(46) Salant and Parkins, *J. Pharmacol. and Exper. Therap.*, 45, 315 (1932).
(47) Rabbeno and Cisbani, *Arch. de internat. Pharmacodyn. et de Thérapie*, 43, 268 (1932).
(48) Epstein, *Ibid.*, 45, 251 (1933).
(49) Bernheim, *Am. J. Physiol.*, 104, 433 (1933).
(50) Hockett, *Newman and Thienes, Arch. de Pharmacodyn. et de Thérapie*, 46, 363 (1933).
(51) Hoyt, Patek and Thienes, *Ibid.*, 47, 228 (1934).
(52) Verzár and McDougall, "Absorption from the Intestine," Longman's, Green and Co., London (1936).
(53) Emerson, *Proc. Soc. Exper. Biol. and Med.*, 35, 376 (1936).
(54) Van Liere and Emerson, *Arch. de internat. Pharmacodyn. et de Thérapie*, 57, 45 (1937).
(55) Reynolds, *Physiol. Rev.*, 17, 304 (1937).
(56) Cheney, *Proc. Soc. Exper. Biol. and Med.*, 37, 572 (1937).
(57) Donatelli, *Arch. de internat. Pharmacodyn. et de Thérapie*, 58, 27 (1938).
(58) Singh, *J. Physiol.*, 94, 1, 322 (1938).
(59) Fischer, *J. Cellular and Comp. Physiol.*, 12, 85 (1938).
(60) Farmer, *Proc. Soc. Exper. Biol. and Med.*, 39, 204 (1938).
(61) McLachlin, *J. Pharmacol. and Exper. Therap.*, 64, 243 (1938).
(62) Lazarus, *J. Physiol.*, 93, Proc. 32-P (1938).
(63) Beard and Pizzolato, *J. Pharmacol. and Exper. Therap.*, 63, 306 (1938).
(64) Franklin and Maher-Loughnan, *J. Physiol.*, 94, 426 (1938).
(65) Eichler, Kaffee und Koffein, *Verlag von J. Springer*, Berlin, 58, 91 (1938).

A STUDY OF THE STABILITY OF ALKALOIDAL POISONS IN THE PRESENCE OF PRESERVATIVES.*

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The stability of alkaloids under various conditions has been the subject of many investigations. Among the more important of these are the very few studies undertaken in the interest of forensic medicine. These deal primarily with the fate of alkaloids when in contact with dead tissue, either preserved with one of several common preserving materials or allowed to decompose. The conditions of contact between the alkaloid and contaminating substance were generally controlled to simulate as nearly as possible one or more actual toxicological situations. One of the earliest investigations of this type carried out was by Tidy (1) who studied the durability of morphine sulfate when exposed to the processes of tissue decomposition within the human body. Little significant work on the stability of alkaloids under circumstances involving legal toxicological investigation has been done since. The recent studeis of Rising and Lynn (2, 3, 4, 5), while dealing in part with alkaloids, were principally on poisons of non-alkaloidal nature.

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In a time when technical evidence in prosecutions of criminal poisonings and litigation over the control of industrial poisoning is of particular importance, there should certainly be more data added to our knowledge concerning the stability of various poisons under all conditions of toxicological interest. Such information concerning alkaloidal poisons would be especially pertinent.

It is to aid in filling these gaps in the field that the following data are presented and their method of collection briefly outlined.

The principal object of the study to be described was to determine the destructive power, if any, on certain poisons, of several substances commonly used by coroners, morticians and others to preserve bodies which might contain a poison. Specimens of viscera are frequently preserved for analysis without thought or knowledge of what effect the preserving agent might have on any poison present. Further, little thought is given to possible interferences in the analytical work due to preservative used. A second object of the study was to investigate this factor.

Since forensic toxicology also involves unembalmed and otherwise unpreserved cadavers, it was deemed highly desirable to determine the stability of poisons in contact with decomposing tissue. Search for such information was made a third phase of the study.

Salts of morphine, codeine, narcotine, pilocarpine, sparteine and veratrine were the poisons chosen for investigation. Cavity fluid, 95 per cent ethyl alcohol, 4 per cent formaldehyde, 1 per cent mercuric chloride and 1 per cent arsenic trioxide were the preservatives selected. Stomachs from freshly killed sheep were made the carriers for the alkaloids.

The specimens for investigation were composed of either the alkaloidal salt in aqueous solution with or without a preservative, or the alkaloidal salt intimately mixed with minced sheep stomach and the mixture covered with a preservative or permitted to decompose. Each sample was contained in a four ounce, clear-glass, wide-mouth bottle closed with a cork and paraffin seal. Certain of the unpreserved samples were left unsealed. All of the unpreserved specimens were allowed to face the exigencies of weather outside. No precaution was taken to keep constant the temperature of those stored inside, nor was the sunlight shut out. Table I shows the conditions to which each alkaloidal salt was subjected.

In order to develop the data desired a complete set of specimens covering each of the conditions under investigation for each poison was analyzed at approximately three-month intervals Tables II to XIII give the results of these determinations.

The methods of extraction and estimation together with a discussion of interfering substances has been presented (6).

TABLE I.

No. of Condition.	Amt. of Alk. Salt.	Volume of Preservative.	Preservative.	Amt. of Sheep Stomach.	Storing Conditions.
1	100.0 mg.	50.0 cc.	Cavity fluid	50.0 Gm.	Sealed
2	100.0 mg.	50.0 cc.	95% alcohol	50.0 Gm.	Sealed
3	100.0 mg.	50.0 cc.	4% HCHO	50.0 Gm.	Sealed
4	100.0 mg.	50.0 cc.	1% As_2O_3	50.0 Gm.	Sealed
5	100.0 mg.	50.0 cc.	1% $HgCl_2$	50.0 Gm.	Sealed
6	100.0 mg.	none	none	50.0 Gm.	Sealed and outside of bldg.
7	100.0 mg.	none		50.0 Gm.	Unsealed and outside of bldg.
8	100.0 mg.	25.0 cc.	Cavity fluid	none	Sealed
9	100.0 mg.	25.0 cc.	95% alcohol	none	Sealed
10	100.0 mg.	25.0 cc.	4% HCHO	none	Sealed
11	100.0 mg.	25.0 cc.	1% As_2O_3	none	Sealed
12	100.0 mg.	25.0 cc.	1% $HgCl_2$	none	Sealed
13	100.0 mg.	25.0 cc.	none	none	Sealed

TABLE II.—STABILITY OF MORPHINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.8	98.6	98.7	98.7	98.0	98.8
3	92.1	93.1	95.0	92.8	94.3	95.2
6	80.4	85.0	86.1	84.3	86.7	89.2
9	76.4	81.2	83.2	79.8	79.3	84.2
12	74.2	77.5	79.3	75.8	75.9	80.5
15	73.5	76.3	77.4	74.3	74.1	78.5
18	71.2	74.3	74.1	72.6	71.7	73.5
21	70.5	73.1	72.5	71.4	70.2	70.1
24	67.7	69.6	68.7	68.8	67.3	68.4

TABLE III.—STABILITY OF MORPHINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	94.8	94.1	96.1	95.7	96.0	96.4	96.4
3	87.2	86.2	87.9	88.0	87.7	91.5	89.2
6	74.0	78.2	80.4	79.3	78.3	78.2	76.7
9	70.2	73.7	72.8	71.5	70.6	73.4	72.4
12	68.3	68.9	68.1	68.3	68.0	76.4	71.3
15	62.7	65.6	66.3	66.1	62.1	68.3	66.7
18	60.6	61.3	61.4	61.7	60.2	63.7	58.8
21	58.2	58.8	59.6	62.1	59.6	59.4	56.9
24	53.7	54.1	56.2	56.3	57.1	55.7	53.2

TABLE IV.—STABILITY OF CODEINE PHOSPHATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.2	98.7	98.7	98.6	98.8	98.8
3	95.5	98.1	98.2	96.3	95.7	98.0
6	94.2	97.7	97.3	95.1	95.4	98.0
9	93.9	97.4	97.0	94.7	95.1	97.6
12	93.4	96.0	96.7	93.5	93.8	97.3
15	92.3	94.7	95.6	92.1	91.9	96.1
18	91.7	93.2	94.8	90.1	91.4	95.3
21	91.4	93.0	94.1	89.3	90.6	94.8
24	90.8	92.7	93.8	88.5	89.4	93.6

TABLE V.—STABILITY OF CODEINE PHOSPHATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	95.3	94.3	95.0	94.2	94.1	94.1	94.1
3	90.6	91.4	90.7	89.2	91.0	89.2	91.7
6	87.2	88.7	86.4	85.7	87.4	86.2	85.6
9	84.6	84.6	83.7	82.2	84.6	83.5	82.4
12	79.4	80.2	82.3	80.7	83.3	79.7	79.8
15	76.3	78.6	79.2	80.3	81.3	78.2	77.1
18	75.5	74.0	78.7	78.9	79.2	76.7	75.2
21	72.4	75.5	76.2	77.5	78.7	74.1	73.6
24	70.1	71.2	72.7	74.3	75.8	70.4	69.3

TABLE VI.—STABILITY OF NARCOTINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.9	98.6	98.7	98.6	98.8	98.7
3	94.4	92.1	94.2	93.1	91.5	96.2
6	87.4	87.2	92.2	90.8	90.2	95.4
9	84.2	85.2	91.0	87.1	88.2	94.2
12	81.0	82.7	89.7	86.4	85.5	93.5
15	77.2	79.3	87.1	84.7	84.0	91.9
18	74.2	77.6	86.2	83.0	82.3	91.5
21	92.5	75.5	84.5	81.2	80.8	91.0
24	71.9	74.0	82.6	78.8	78.7	89.7

TABLE VII.—STABILITY OF NARCOTINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.1	95.1	93.7	94.6	94.2	95.0	95.0
3	85.1	89.1	88.6	90.0	89.1	90.3	89.5
6	78.2	81.3	82.7	84.7	80.8	82.4	83.1
9	71.4	74.1	75.0	77.9	74.3	75.9	76.5
12	65.3	71.8	70.7	72.4	70.8	71.3	71.2
15	60.0	64.7	66.5	66.8	67.4	66.5	66.7
18	51.6	60.3	64.0	61.7	63.1	63.7	62.4
21	47.5	58.6	56.8	58.1	58.3	59.6	56.8
24	44.2	55.8	53.6	54.7	55.5	54.4	53.2

TABLE VIII.—STABILITY OF PILOCARPINE NITRATE IN CONTACT WITH PRESERVATIVE SOLUTION

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.6	98.7	98.9	98.8	98.1	98.8
3	93.2	94.1	96.1	95.7	96.0	95.4
6	88.0	98.6	92.7	94.0	92.3	91.1
9	85.6	86.2	89.2	93.8	89.4	87.4
12	83.4	83.2	88.5	93.3	87.7	85.1
15	82.2	82.7	87.1	91.2	86.2	84.2
18	80.2	81.8	84.4	90.1	86.0	83.3
21	77.7	80.5	82.1	89.5	83.0	82.0
24	76.5	78.7	81.6	87.2	81.0	81.3

TABLE IX.—STABILITY OF PILOCARPINE NITRATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.3	94.0	94.5	93.7	95.1	94.2	94.2
3	85.2	87.6	87.5	88.2	87.7	88.3	87.4
6	77.3	76.8	78.4	80.1	76.9	77.1	76.2
9	67.5	68.6	72.4	73.6	71.3	72.7	70.6
12	62.4	64.7	66.7	68.0	65.6	64.8	67.2
15	58.7	59.1	62.8	61.7	61.1	60.3	62.4
18	53.8	55.3	57.3	57.4	57.6	56.8	55.3
21	47.6	53.8	54.6	54.1	54.7	52.5	52.1
24	43.2	49.7	51.2	52.8	50.9	49.4	51.7

TABLE X.—STABILITY OF SPARTEINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.5	98.7	98.8	98.7	98.1	98.8
3	95.2	96.3	96.3	97.1	94.3	95.6
6	93.3	93.7	93.5	94.3	90.9	91.1
9	90.6	92.1	91.7	93.6	89.4	91.0
12	88.1	90.4	91.2	93.2	90.3	90.3
15	84.6	87.3	89.8	92.5	88.8	90.2
18	79.4	86.7	88.1	92.4	87.2	90.0
21	77.1	83.5	86.5	90.2	85.0	89.3
24	75.3	83.5	85.1	89.4	84.2	88.1

TABLE XI.—STABILITY OF SPARTEINE SULFATE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.1	94.3	94.8	94.9	94.1	95.1	95.1
3	83.5	88.2	87.3	86.4	87.3	88.7	89.1
6	72.4	77.5	78.3	79.3	79.0	78.5	76.4
9	66.7	68.2	68.5	69.5	72.4	70.4	69.3
12	57.3	62.3	60.2	62.6	67.7	64.4	65.7
15	50.1	57.8	56.7	58.5	61.5	57.9	58.3
18	45.7	55.2	52.5	52.7	54.6	53.6	52.6
21	40.2	52.3	49.7	46.1	49.8	48.7	48.5
24	38.7	48.2	47.5	44.7	47.4	46.1	45.7

TABLE XII.—STABILITY OF VERATRINE HYDROCHLORIDE IN CONTACT WITH PRESERVATIVE SOLUTION.

Months.	Per Cent of Recovery.					
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Water.
0	98.6	98.6	98.8	98.8	98.7	98.8
3	95.3	96.1	96.0	95.6	95.4	94.8
6	93.6	93.5	94.7	94.1	93.5	92.2
9	90.4	91.7	91.0	92.5	91.9	91.4
12	89.6	89.2	90.3	91.0	90.2	91.2
15	87.4	88.3	89.7	89.8	89.8	89.4
18	86.1	86.7	88.3	87.6	87.3	88.2
21	84.7	85.2	86.7	87.7	85.6	86.7
24	84.1	83.0	85.1	86.4	84.7	86.3

TABLE XIII.—STABILITY OF VERATRINE HYDROCHLORIDE IN CONTACT WITH PRESERVATIVE SOLUTION AND ANIMAL TISSUE.

Months.	Per Cent of Recovery.						
	$HgCl_2$.	HCHO.	As_2O_3.	Alc.	Cav. Flu.	Exp.	Unexp.
0	93.3	95.8	94.1	95.1	94.6	96.2	96.2
3	87.2	88.7	90.1	91.7	91.2	91.9	90.4
6	84.1	85.6	87.6	87.8	86.3	87.1	87.8
9	80.0	81.2	86.7	83.6	81.5	82.3	85.7
12	75.7	76.6	82.3	80.1	77.6	89.1	80.2
15	72.4	72.7	76.5	75.3	74.2	77.8	77.1
18	68.6	69.1	74.3	72.4	71.8	73.6	72.8
21	64.3	66.5	72.9	69.8	69.0	72.3	70.7
24	62.4	65.3	71.4	68.4	69.7	70.2	69.8

TABLE XIV.—BEST PRESERVATIVE FOR ALKALOIDAL SALT IN SOLUTION.

Alkaloidal Salt.	Preservative.	Per Cent of Alkaloidal Salt Remaining at End of 2 Years.
Morphine Sulfate	4% formaldehyde	69.6
Codeine Phosphate	1% arsenic trioxide	93.8
Narcotine Sulfate	1% arsenic trioxide	82.6
Pilocarpine Nitrate	95% alcohol	87.2
Sparteine Sulfate	95% alcohol	89.4
Veratrine Hydrochloride	95% alcohol	86.4

TABLE XV.—POOREST PRESERVATIVE FOR ALKALOIDAL SALT IN SOLUTION.

Alkaloidal Salt	Preservative.	Per Cent of Alkaloidal Salt Remaining at End of 2 Years.
Morphine Sulfate	Cavity fluid	67.3
Codeine Phosphate	95% alcohol	88.5
Narcotine Sulfate	1% mercuric chloride	71.9
Pilocarpine Nitrate	1% mercuric chloride	76.5
Sparteine Sulfate	1% mercuric chloride	75.3
Veratrine Hydrochloride	4% formaldehyde	83.0

TABLE XVI.—BEST PRESERVATIVE FOR ALKALOIDAL SALTS IN CONTACT WITH ANIMAL TISSUE.

Alkaloidal Salt.	Preservative.	Per Cent of Alkaloidal Remaining at End of 2 Years.
Morphine Sulfate	Cavity fluid	57.1
Codeine Phosphate	Cavity fluid	75.8
Narcotine Sulfate	4% formaldehyde	55.8
Pilocarpine Nitrate	95% alcohol	52.8
Sparteine Sulfate	4% formaldehyde	48.2
Veratrine Hydrochloride	1% arsenic trioxide	71.4

TABLE XVII.—POOREST PRESERVATIVE FOR ALKALOIDAL SALTS IN CONTACT WITH ANIMAL TISSUE.

Alkaloidal Salt.	Preservative.	Per Cent of Alkaloidal Remaining at End of 2 Years.
Morphine Sulfate	1% mercuric chloride	53.7
Codeine Phosphate	1% mercuric chloride	70.1
Narcotine Sulfate	1% mercuric chloride	44.2
Pilocarpine Nitrate	1% mercuric chloride	43.2
Sparteine Sulfate	1% mercuric chloride	38.7
Veratrine Hydrochloride	1% mercuric chloride	62.4

SUMMARY

Data are presented showing the stability of morphine sulfate, codeine phosphate, narcotine sulfate, pilocarpine nitrate, sparteine sulfate and veratrine hydrochloride under various toxicological conditions.

REFERENCES.

(1) Tidy, *Med. Times and Gaz.*, 1, 497 (1868); Witthaus and Becker, *Medical Jurisprudence, Forensic Medicine and Toxicology*, Vol. 4.

(2) Rising and Lynn, JOUR. A. PH. A., 20, 9 (1931).

(3) Rising and Lynn, *Ibid.*, 21, 138 (1932).

(4) Rising and Lynn, *Ibid.*, 21, 225 (1932).

(5) Rising and Lynn, *Ibid.*, 21, 334 (1932).

(6) Wilson and Rising, *Ibid.*, 28, 146 (1939).

SALTS OF TRIETHANOLAMINE. II. DETERGENCY.*

BY GEORGE W. FIERO.[1]

Fatty acid salts of triethanolamine have been suggested as substitutes for soap in both commercial and cosmetic use because of their low alkalinity as compared with ordinary soaps. The various salts of triethanolamine with pure fatty acids (1) were subjected to washing tests to determine their relative efficiency.

Apparatus.—In order to determine the relative soil of the cloth employed in the washing tests, a photoelectric photometer was devised. This consisted of, as illustrated in Fig. 1, a photoelectric cell (Weston Photronic Cell No. 594) mounted in a box opposite a tubular 100 watt projection bulb. The two were separated by a partition of insulating material extending to within 1 cm. of the top of the container. This partition was movable so that optimum reflection could be obtained and then firmly fixed in this position. In order that the illumination from the bulb be identical in the tests, the voltage of the current was measured at each experiment and adjusted uniformly. The temperature was kept uniform by means of a fan near the top of the bulb which removed the warm air from both the bulb and the cell. The cell was connected in series with a microammeter so that the amount of current produced could be measured.

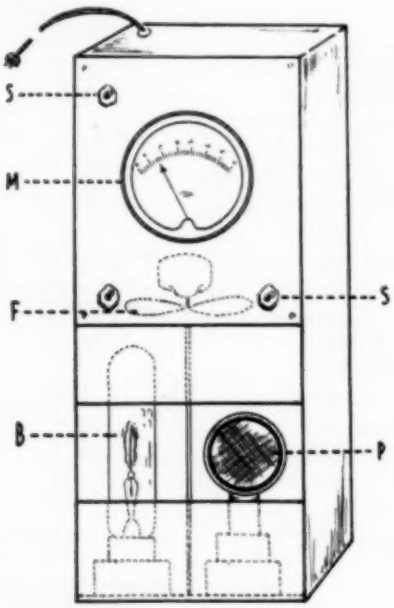

Fig. 1.---PHOTOELECTRIC PHOTOMETER
B-projection bulb, P-photoelectric cell,
M-microammeter, F-fan, - S-switch.

In order to test the extent of soil of a sample of cloth, it was folded longitudinally and held firmly across the opening above the bulb and the cell so that light would be reflected to the cell and the extent of reflected light measured as microamperes. The extent of soil would be indicated by the relative amount of light absorbed. A clean cloth was taken as standard for 0% soil and a photographic plate cover was used as a standard for 100% soil. The difference in microamperes between the two readings was divided by 100 to give data in per cent. While this is not exactly correct, for practical purposes it gave a readily obtainable measure of relative extent of soil. This apparatus has certain advantages over optical photometers in that it is less expensive and that a larger surface of soiled cloth is measured with each determination.

The apparatus for washing the cloth consisted of four wide mouth ("Mason") jars held in an aluminum frame within the agitator of a *Whirldry* miniature washing machine. The temperature was maintained by means of warm water filling the tank and covering the jars. The bottles moved over an arc of 90° and completed oscillation 80 times per minute.

EXPERIMENTAL.

Recently ironed white cotton cloth (thread count 80 x 80 per inch), 6 x 9 inches, was soiled with artificial soil mixture, dried at 80° C. for one hour, aged over night, ironed with a low-heat iron and the extent of soil determined. Eight readings were taken with each cloth so as to cover

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a large area of both sides. Two samples were placed in 200 cc. of a one per cent solution of the triethanolamine salt and washed for 10 minutes at 45° C. The cloth was removed, rinsed in distilled water three times, partially dried on bibulous paper, placed in oven at 80° for one hour and finally dried in air for 30 minutes. The cloth was then ironed and the extent of soil determined. The soil mixture (2) consisted of:

Lamp Black	2 Gm.
Liquid Petrolatum, heavy	5 Gm.
Tallow	3 Gm.
Carbon Tetrachloride	2000 cc.

Four cloths were washed with each salt; the average readings of the four samples is shown in the table below:

Salt of Triethanolamine.	Original Soil.	First Wash.	Soil Removed.	Second Wash.	Soil Removed.
Caproate	36.7%	23.2%	13.5%	18.8%	17.9%
Isocaproate	36.4%	22.7%	13.7%	18.4%	18.0%
Caprylate	35.7%	19.0%	16.7%	16.4%	19.3%
Caprate	37.0%	18.4%	18.6%	14.4%	22.6%
Laurate	36.7%	8.3%	28.4%	5.9%	30.8%
Myristate	36.7%	9.5%	27.2%	7.4%	29.3%
Palmitate	36.7%	11.3%	25.4%	6.9%	27.8%
Stearate	36.6%	17.7%	18.9%	15.8%	20.8%
Oleate	36.8%	8.9%	27.7%	6.4%	30.4%

Commercial Fatty Acids.—The preceding tests were made with soaps prepared from pure (Eastman) fatty acids. Salts were also prepared from commercial mixed fatty acids used in the manufacture of soap. These were prepared by heating equivalent molecular quantities (based upon the acid value of the mixed fatty acids) of triethanolamine and fatty acid. Salts were prepared from the mixed fatty acids of tallow, cocoanut oil and red oil; the latter is equivalent to the mixed fatty acids of olive oil.[1]

Four cloths were washed in the same manner as above with each of the soaps; the average readings of the four samples is shown in the table below:

Salt of Fatty Acid.	Acid Value.[1]	Original Soil.	First Wash.	Soil Removed.	Second Wash.	Soil Removed.
Coconut Oil	265.5	30.0%	14.3%	15.7%	8.3%	21.7%
Tallow	198.5	29.5%	13.9%	15.6%	6.1%	23.4%
Red Oil	195.0	30.2%	16.4%	13.8%	9.2%	21.0%

SUMMARY.

An apparatus is described utilizing a photoelectric cell to determine the extent of soil of cloth. Pure salts of triethanolamine were subjected to washing tests. The following salts had definite detergent action: laurate, oleate, myristate, palmitate (in order named). None of these salts possessed as great a detergent action as ordinary soap. Triethanolamine salts of commercial mixed fatty acids possessed detergent action in the order named: tallow fatty acids, cocoanut oil fatty acids, red oil.

REFERENCES.

(1) Fiero, G. W., Jour. A. Ph. A., 27, 658 (1938).
(2) Rhodes, F. H., and Brainard, S. W., *Ind. Eng. Chem.*, 21, 61 (1929).

[1] The writer is indebted to the Research Laboratories of Proctor and Gamble Company for samples.

THE MERCURATION OF SUBSTITUTED DERIVATIVES OF THYMOL.*,1

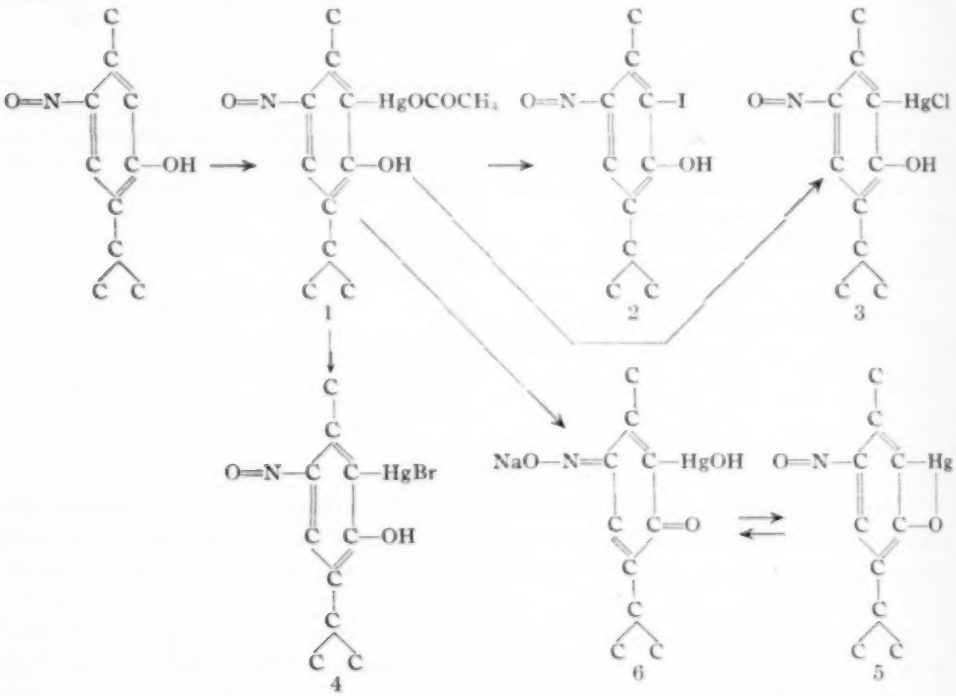
BY A. WAYNE RUDDY[2] AND JOSEPH B. BURT.[3]

I. Nitrosothymol Derivatives.

Inasmuch as one of the authors (1) of this paper had previously reported upon some of the mercury derivatives of carvacrol and thymol, it appeared to be worthwhile to investigate the reaction of mercuric acetate upon some of the substituted derivatives of these phenols. It was originally proposed that the reaction be applied to nitrosothymol, nitrosocarvacrol and chlorthymol. Surprisingly enough, negative results were obtained in a number of attempts to form mercury derivatives of nitrosocarvacrol, although no difficulty was experienced in obtaining derivatives from the other two compounds.

EXPERIMENTAL.

The 6-nitrosothymol used in these experiments was prepared according to the method of Kremers, Wakeman and Hixon (2), purified by dissolving in dioxan and precipitating by the addition of petroleum ether. The derivatives which were formed are shown graphically below, with the number under each compound corresponding to the number of the section which follows describing that compound.



* Presented before the Scientific Section, A. Ph. A., Minneapolis meeting, 1938.

[1] A portion of a thesis submitted in partial fulfilment of the requirements for the degree of Master of Science, University of Nebraska, 1938.

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1. 2-Acetoxymercuri-6-nitrosothymol.—Thirty-five and six-tenths grams of reagent mercuric acetate were dissolved with heating in 1 L. of alcohol containing 0.8 per cent of acetic acid, and 20 Gm. of 6-nitrosothymol were added. The reaction mixture, which was in equimolecular proportions, was refluxed on a steam-bath during four hours. A sample of the reaction mixture, when tested with sodium hydroxide test solution gave a black precipitate of mercurous oxide, but no evidence of mercuric oxide, indicating the absence of mercuric acetate and the presence of some mercurous acetate. The mixture was concentrated under reduced pressure to about three-fourths of the original volume, at which point a small amount of crystalline precipitate, later identified as mercurous acetate, was formed. This was removed from the hot liquid by suction filtration. The filtrate, upon being chilled with ice, deposited a semi-solid mass which was filtered out with suction and washed with a small quantity of cold alcohol. Yellow needles, arranged in tufts, and weighing 39.2 Gm. were obtained. Upon analysis these were found to contain 49.77 per cent of mercury, whereas the calculated percentage for this compound is 45.82 per cent. The product was evidently contaminated with inorganic mercury compounds.

For the purpose of purification 33 Gm. of the impure compound were dissolved in 200 cc. of 3.5 per cent solution of sodium hydroxide. Upon filtration a yellow and black residue of mercuric and mercurous oxides was obtained, and a clear, deep red solution. The latter was poured with stirring into 500 cc. of distilled water containing 12 cc. of glacial acetic acid, yielding a light yellow, flocculent precipitate. When filtered with suction, washed with water and air-dried, a light yellow, amorphous powder was obtained weighting 22 Gm. When recrystallized from 95 per cent alcohol containing a trace of acetic acid, bright yellow needles were obtained weighing 21.5 Gm. This represented 52.3 per cent of the theoretical yield. Two samples gave upon analysis 45.80 and 45.97 per cent of mercury. The theoretical value for this compound ($C_{12}H_{15}O_4NHg$) is 45.82 per cent.

A second reaction carried out in the same way, using three moles of mercuric acetate to one mole of nitrosothymol and refluxed during four and one-half hours, failed to produce any evidence of a dimercurated compound, but the yield of 2-acetoxymercuri-6-nitrosothymol was increased to 73.9 per cent of the theoretical.

2-Acetoxymercuri-6-nitrosothymol is slightly soluble in cold alcohol, readily soluble in hot alcohol, and slightly soluble in other volatile solvents such as benzene, ether and acetone. It dissolves easily and is quite stable in dilute alkali solutions. It is relatively stable in cold dilute acids, but the mercury group is readily removed by heating in acid solutions. When heated rapidly it darkens at 145° C. and melts with decomposition at 147.5° C.

2. 2-Iodo-6-nitrosothymol.—To 5 Gm. of 2-acetoxymercuri-6-nitrosothymol in 50 cc. of glacial acetic acid 4.3 Gm. of iodine were added and the mixture was heated on a steam-bath for one hour. A precipitate of red mercuric iodide formed in the bottom of the flask. The supernatant liquid was decanted and then diluted to 1 L. by the addition of distilled water, which caused the nitrosothymol derivative to precipitate. The latter was found upon removal by suction filtration to lack uniformity because of contamination with a dark-colored substance. It was purified by dissolving in dilute sodium hydroxide solution, filtering and pouring the dark red filtrate into a dilute hydrochloric acid solution. The resulting precipitate was filtered out with suction and washed with water until free from chlorides, and appeared as a yellow, amorphous powder. By recrystallization from benzene 1.9 Gm. of dark yellow needles were obtained which darkened at 127° C. and melted sharply at 130° C. The calculated yield is 54.6 per cent of the theoretical. Kehrmann (3) describes 2-iodo-6-nitrosothymol as melting and decomposing with rapid heating at 129° C.

3. 2-Chlormercuri-6-nitrosothymol.—A second quantity of 2-acetoxymercuri-6-nitrosothymol was prepared using the same quantities of reactants and following the procedure previously described. After filtering the hot reaction mixture to remove traces of mercurous acetate which had formed, the solution was poured slowly with stirring into 4 L. of 0.65 per cent aqueous solution of sodium chloride. A cream-colored, flocculent precipitate was formed which, after standing six hours, was filtered out with suction and washed with water until free from chlorides, as shown by silver nitrate test solution. In making this test the nitric acid was added last and the observation made immediately afterward. Otherwise, it was found that the acid upon standing hydrolyzed enough of the compound to give a positive test for chlorides. After drying, 32.5 Gm. of a light buff or cream-colored, amorphous powder were obtained. About 27 Gm. of the compound

were recrystallized from hot, 70 per cent alcohol, yielding 18.2 Gm. of light yellow needles, which represented 47.4 per cent of the theoretical yield. Upon analysis two samples gave 48.93 and 48.95 per cent of mercury. The theoretical percentage for this compound ($C_{10}H_{12}O_2NHgCl$) is 48.43 per cent of mercury.

4. 2-Brommercuri-6-nitrosothymol.—Fifty-three and four-tenths grams of mercuric acetate were dissolved in 800 cc. of alcohol containing 2 per cent acetic acid and 20 Gm. of 6-nitrosothymol were added. This represented a reaction ratio of one and one-half moles of mercuric acetate to one mole of nitrosothymol. After refluxing on a steam-bath for a period of four and one-half hours, the hot reaction mixture after being filtered to remove a small quantity of mercurous acetate, was chilled with ice. Two crops of impure 2-acetoxymercuri-6-nitrosothymol, weighing 40.5 and 1.2 Gm. respectively, were obtained. Eight grams of unreacted nitrosothymol were recovered from the mother liquor.

To remove impurities from the combined precipitates, they were dissolved in 200 cc. of 4 per cent sodium hydroxide solution and the resulting solution was filtered with suction. The residue which failed to dissolve weighed 8.5 Gm. and consisted of a mixture of mercurous and mercuric oxides.

The clear, deep-red filtrate was poured slowly with stirring into a mixture of 40 cc. of 40 per cent hydrobromic acid with 500 cc. of distilled water, and yielded a light yellow, bulky precipitate which was filtered out with suction and washed with water. When dried in the air 29.5 Gm. of light yellow, amorphous powder were obtained. When recrystallized from 95 per cent alcohol two crops of 2-brommercuri-6-nitrosothymol were obtained as small, light yellow needles, weighing 17.0 and 8.0 Gm. respectively. This represented 48.8 per cent of the theoretical yield. Two samples gave upon analysis 43.73 and 43.54 per cent of mercury. The theoretical percentage for this compound ($C_{10}H_{12}O_2NHgBr$) is 43.73 per cent of mercury.

2-Brommercuri-6-nitrosothymol is very slightly soluble in water, slightly soluble in cold alcohol, readily soluble in hot alcohol and somewhat soluble in other volatile solvents. It dissolves readily in solutions of alkalies giving a deep red solution without hydrolysis. It is stable in cold dilute acids, but application of heat to the acid mixture readily removes the mercury group. When heated rapidly it darkens at 148° C. and melts with decomposition at 152–153° C.

5. Thymol-2-(hydroxymercuri)-6-nitroso-oxide.—Ten grams of 2-acetoxymercuri-6-nitrosothymol were dissolved in 3 per cent sodium hydroxide solution, producing a clear, deep red solution. This was diluted with about 500 cc. of distilled water and carbon dioxide was passed into the solution until no further precipitation occurred. The precipitate was filtered out with suction and washed until the washings were neutral to litmus and free from acetates. A bright yellow, amorphous powder was obtained which in the air-dried condition weighed 8.5 Gm. This was practically a quantitative yield. Upon analysis two samples gave 53.74 and 53.23 per cent of mercury. Theoretically this compound ($C_{10}H_{11}O_2NHg$) should contain 53.10 per cent of mercury.

The oxide linkage is readily opened when treated with dilute alkalies, but the mercury remains firmly attached to the nucleus. The compound is stable in cold acids, but heating in dilute acids readily hydrolyzes the mercury group. The substance is practically insoluble in water, and only slightly soluble in the common volatile solvents. When heated rapidly it begins to darken at 204° C. and melts sharply with decomposition at 210° C.

6. Sodium-2-hydroxymercuri-6-isonitrosothymoquinone.—A sample of thymol-2-(hydroxymercuri)-6-nitroso-oxide was added to a 5 per cent solution of sodium hydroxide to effect cleavage of the oxide linkage and formation of sodium hydroxymercuri isonitrosothymoquinone. The compound dissolved readily in the alkali solution, producing a clear, deep red solution When this solution was allowed to evaporate spontaneously a red-brown, amorphous compound was obtained which was assumed to be the sodium salt of 2-hydroxymercuri-6-isonitrosothymoquinone. It is extremely soluble in water in this form. It is fairly stable but when allowed to stand for several days, it gradually undergoes a change. It finally becomes yellowish green in color and is then practically insoluble in water.

NITROSOCARVACROL.

A number of attempts to mercurate-5-nitrosocarvacrol were made, but in all cases negative results were obtained. The conditions employed in these attempts are summarized below:

Solvent.	Nitroso-carvacrol.	Mercuric Acetate.	Molecular Ratio.	Time.
(1) 500 cc. alcohol + 8 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	4 hrs.
(2) 250 cc. alcohol + 8 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	5 hrs.
(3) 125 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	4 hrs.
(4) 1000 cc. alcohol + 25 cc. glacial acetic acid	20 Gm.	106.7 Gm.	1:3	8 hrs.
(5) 125 cc. cellusolve + 5 cc. glacial acetic acid	10 Gm.	17.8 Gm.	1:1	½ hr.

ANALYTICAL.

The initial attempts to analyze these compounds for mercury content included a decomposition of the samples with concentrated sulfuric and nitric acids as outlined in the procedure given for the assay of mercuric salicylate in the Pharmacopœia of the United States (4). The inorganic mercury contained in the resulting acid solution was then precipitated as mercury zinc thiocyanate according to the procedure of Jamieson (5). It was found however, that in order to insure consistent results a very careful adjustment of the acid concentration was necessary. For this reason another method was adopted.

A method suggested by Weitkamp (6) in which the mercury was split off by hydrobromic acid was modified to some extent and found to be very satisfactory. The procedure was as follows: Approximately a half-gram sample was weighed accurately and transferred to a 250-cc. Erlenmeyer flask. The sides of the flask were washed down with 25 cc. of alcohol and 10 cc. of concentrated hydrocloric acid were added. The mixture was boiled under a reflux condenser for about forty-five minutes. The solution, after cooling was diluted with alcohol and water to a volume of about 60 cc. The amount of alcohol in the solution varied from 50 to 80 per cent, depending upon the solubility of the organic residue of the substance being analyzed. After treatment with hydrogen sulfide the precipitate of mercuric sulfide was transferred to a tared fritted crucible and washed with alcohol, followed by two successive extractions with carbon tetrachloride, to insure the removal of any sulfur that might have been precipitated. The precipitate was washed once again with alcohol, dried at 120° C. and weighed.

DISCUSSION.

The procedure described for the substitution of iodine for the acetoxymercuri group is acetoxymercuri nitrosothymol resulting in the formation of 2-iodo-6-nitrosothymol, previously described by Kehrmann (3) affords proof that the mercury group occupies position 2, in this compound. Since the other mercury derivatives described above have all been derived through the acetoxymercuri derivative, it follows that these compounds also contain the mercury group in the same position.

The failure to obtain mercury derivatives of nitrosocarvacrol is rather difficult to explain. Since the two position isomers, thymol and carvacrol apparently may be mercurated with equal ease, it would normally be assumed that nitrosocarvacrol should react as readily as nitrosothymol. It is always possible to attribute such behavior to steric hindrance, but not completely satisfactory. It is probable that mercuration of nitrosocarvacrol may be accomplished if the necessary conditions can be found.

It is rather significant to note that in the mercuration of nitrosothymol only mono-derivatives were obtained, whereas even in using equimolecular proportions of thymol and mercuric acetate, traces or more of the dimercury derivative have always been found.

SUMMARY.

(1) 6-Nitrosothymol was mercurated by means of mercuric acetate in alcoholic solution and yielded 2-acetoxymercuri-6-nitrosothymol.

(2) The acetoxymercuri derivative was used to prepare 2-chlormecuri-6-nitrosothymol, 2-brommercuri-6-nitrosothymol and thymol-2-(hydroxymercuri)-6-nitroso-oxide.

(3) Sodium 2-hydroxymercuri-6-isonitrosothymoquinone was produced from the oxide by the action of sodium hydroxide.

(4) The position of the mercury group was proved by replacement of mercury with iodine and identification of the derivative as 2-iodo-6-nitrosothymol.

(5) Several attempts to introduce mercury into the nucleus of 5-nitrosocarvacrol were unsuccessful.

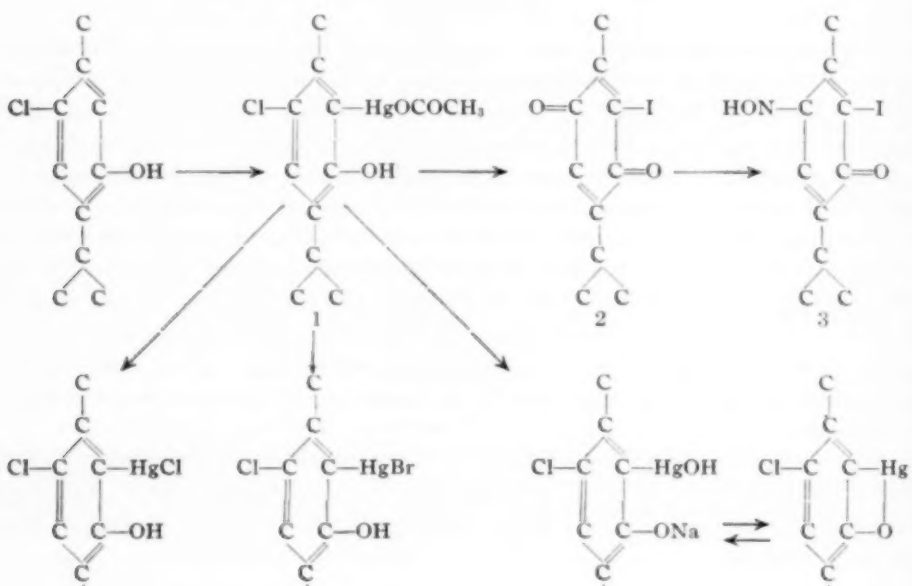
REFERENCES.

(1) Burt, J. B., Jour. A. Ph. A., 25, 112 (1936).
(2) Kremers, E., Wakeman, N., and Hixon, R. M., "Organic Synthesis" VI, 92 (1926), Collective Volume I, 498 (1932).
(3) Kehrmann, Fr., *J. prak. Chem.*, (2), 39, 395 (1889).
(4) Pharmacopœia of the United States of America, Eleventh Revision, page 189 (1936)
(5) Jamieson, G. S., *Ind. & Eng. Chem.*, II, 4, 296 (1919).
(6) Weitkamp, A. W., Unpublished thesis, University of Nebraska, July 13, 1937.

II. Chlorthymol Derivatives.

EXPERIMENTAL.

The derivatives which were formed are shown below graphically, with the number under each compound corresponding to the section which follows describing that compound.



1. 2-Acetoxymercuri-6-chlorthymol.—To 34.5 Gm. of reagent mercuric acetate contained in 500 cc. of alcohol containing 8 cc. of glacial acetic acid 20 Gm. of 6-chlorthymol (N. F. VI) were added. This was an equimolecular ratio of mercuric acetate and chlorthymol. The mixture was refluxed on a steam-bath for four and one-half hours, at the end of which time a small amount of crystalline material had started to form. The reaction mixture was chilled, filtered with suction and washed with a small amount of cold alcohol. A white crystalline product was obtained, weighing 36.4 Gm. Upon concentration of the mother liquor under reduced pressure and chilling a second crop of 4.8 Gm. was obtained.

When a sample of the compound was treated with cold dilute alkali, it gave a slight precipitate of mercurous oxide which indicated that it was contaminated with mercurous acetate. The combined precipitates were therefore dissolved in 200 cc. of 4 per cent sodium hydroxide solution. The residue of mercurous oxide was removed by suction filtration, and the clear, colorless filtrate was poured with stirring into 500 cc. of 4 per cent acetic acid. The white, flocculent precipitate which was formed was filtered with suction and washed several times with distilled water. A slighly pink, amorphous powder was obtained, weighing 35.5 Gm. When recrystallized from alcohol containing a little acetic acid 32.3 Gm. of white, lustrous, monoclinic prisms in the form of plates were obtained. This represents 67.2 per cent of the theoretical yield. Two samples, upon analysis gave 45.53 and 45.59 per cent of mercury. The calculated value for this compound ($C_{12}H_{15}O_3HgCl$) is 45.25 per cent.

When a second reaction was carried out in a similar manner, using one mole of chlorthymol to three moles of mercuric acetate, there was no evidence of dimercuration. However, the yield was increased to 73.8 per cent of the theoretical.

2-Acetoxymercuri-6-chlorthymol is very slightly soluble in water, slightly soluble in cold alcohol and readily soluble in hot alcohol. It requires the presence of a slight amount of acetic acid when in solution to stabilize the acetoxymercuri group. It dissolves readily and is quite stable in dilute alkalies. It is stable in cold dilute acids, but when heat is applied the mercury group is easily removed. When heated rapidly it begins to darken at 173° C., and melts with decomposition at 175–176° C.

2. 2-Iodothymoquinone.—For the purpose of determining the position in which the mercury group enters the nucleus of chlorthymol, the following procedure was carried out: To 8 Gm. of 2-acetoxymercuri-6-chlorthymol in 50 cc. of glacial acetic acid 6.9 Gm. of iodine were added, and the mixture allowed to react at room temperature with frequent shaking for several hours. A clear, yellow liquid was formed and a precipitate of red mercuric iodide settled on the bottom of the flask. The liquid containing 2-iodo-6-chlorthymol was decanted and treated with chromic acid as described by Bordeianu (1). This treatment produced a yellow-orange liquid which remained on the bottom of the flask. The reaction mixture, upon steam distillation, produced an amber-colored oily distillate, which after chilling for several hours yielded a red-orange crystalline mass.

When recrystallized from 80 per cent alcohol, the substance was obtained as yellow-orange masses of needles weighing 1.7 Gm. This compound showed the presence of iodine in a sodium decomposition reaction and possessed an odor and color resembling those of thymoquinone. Although it did not dry readily in the air, after drying for twenty-four hours in a vacuum desiccator it melted at 59° C.

Kehrmann (2) describes this compound as melting at 60–61° C. Bordeianu (1) gives a melting point of 61° C.

3. 2-Iodo-6-isonitrosothymoquinone. (2-Iodo-6-nitrosothymol).—In order to further confirm the identity of the 2-iodothymoquinone, a small sample was treated with hydroxylamine hydrochloride in accordance with the method given by Kamm (3). The resulting product should be the oxime or isonitroso derivative of 2-iodothymoquinone. This is tautomeric with 2-iodo-6-nitrosothymol. After purification the compound in the form of dark yellow needles was found to darken at 127° C. and melt at 130° C. Kehrmann (4) reports 2-iodo-6-nitrosothymol as melting and decomposing with rapid heating at about 130° C.

4. 2-Chlormercuri-6-chlorthymol.—Thirty-four and five-tenths grams of mercuric acetate were dissolved in 450 cc. of alcohol and 8 cc. of glacial acetic acid. Twenty grams of chlorthymol were added and the mixture refluxed on a steam-bath during four hours. The small amount of mercurous acetate which had formed was removed by filtering the hot solution with suction. The filtrate, while hot, was poured slowly, with stirring into 4 L. of 0.65 per cent solution of sodium

chloride. A milky suspension was formed at first but upon continued stirring a flocculent precipitate settled out. After standing three hours the precipitate was removed by suction filtration and washed with distilled water. Thirty-eight and seven-tenths grams of a flesh-colored amorphous powder were obtained.

This impure 2-chlormercuri-6-chlorthymol when recrystallized from 70 per cent alcohol yielded 31.5 Gm. of a mixture of cream-colored crystals and a powder having the appearance of the substance before recrystallization. Upon concentration of the mother liquor under reduced pressure 3.5 Gm. of a buff-colored, crystalline compound were obtained. The combined precipitates were heated in 70 per cent alcohol with activated carbon, filtered and the solution was chilled. Thirty-three and three-tenths grams of a white, crystalline compound were obtained which corresponds to 73.3 per cent of the theoretical yield. Two samples gave upon analysis 47.86 and 47.99 per cent of mercury. The calculated value for this compound ($C_{10}H_{12}OHgCl_2$) is 47.80 per cent of mercury.

This compound behaves toward the various solvents in much the same manner as the acetoxymercuri derivative. It appears to be sensitive to light as it tends to darken on prolonged exposure. It is readily soluble and quite stable in dilute solutions of alkalies. It is stable in cold dilute acids but readily loses the mercury group when heat is applied. When heated rapidly it melts sharply with decomposition at 165° C.

5. 2-Brommercuri-6-chlorthymol.—Twenty grams of chlorthymol were converted into the acetoxymercuri derivative in much the same manner as described above, except that one and one-half moles of mercuric acetate were used for each mole of chlorthymol. The hot solution of the acetoxymercuri derivative was poured slowly with stirring into 5 L. of 0.7 per cent solution of sodium bromide. The flocculent precipitate which was formed was filtered with suction and washed with distilled water to remove the excess sodium bromide and the unreacted mercuric acetate. A light cream-colored powder was obtained, weighing 46.3 Gm. Upon recrystallization from 70 per cent alcohol, two crops of light cream-colored crystals were obtained, weighing 40.5 Gm. and 2.5 Gm. respectively. These combined crops were again recrystallized from 95 per cent alcohol and yielded 38.4 Gm. of 2-brommercuri-6-chlorthymol as large, white crystals. This weight represents 75.7 per cent of the theoretical yield. Two samples upon analysis showed 43.46 and 43.31 per cent of mercury. The calculated value for this compound ($C_{10}H_{12}OHgClBr$) is 43.22 per cent of mercury.

2-Brommercuri-6-chlorthymol is very slightly soluble in water, slightly soluble in cold alcohol and readily soluble in hot alcohol. It appears to be somewhat sensitive to light as it tends to darken upon prolonged exposure. It is readily soluble and quite stable in dilute solutions of alkalies. It is stable in the presence of dilute acids in the cold, but readily loses its mercury group when heat is applied. When the compound is heated rapidly it melts sharply with decomposition at 156° C.

6. Thymol-2-(hydroxymercuri)-6-chlor-oxide.—Ten grams of 2-acetoxymercuri-6-chlorthymol were dissolved in the cold in 85 cc. of 3 per cent sodium hydroxide solution, producing a clear, colorless solution. After dilution to about 500 cc. with distilled water, carbon dioxide was passed into the solution until no further precipitation occurred. The precipitate was removed by suction filtration and washed thoroughly with distilled water to remove the sodium acetate and sodium bicarbonate which had been formed in the reaction. Eight and four-tenths grams of a white amorphous powder were obtained. This was practically a quantitative yield. Two samples, upon analysis showed 52.29 and 52.17 per cent of mercury. The calculated value for this compound ($C_{10}H_{11}OHgCl$) is 52.34 per cent of mercury.

This compound when treated with alkali resists the opening of the oxide linkage much more strongly than does the corresponding thymol-2-(hydroxy-mercuri)-6-nitroso-oxide. Application of heat to the alkaline mixture appears to aid in the cleavage of this linkage but even continued heat fails to completely dissolve the compound. The oxide is stable in cold dilute acids, but readily loses its mercury group when the acid mixture is heated. It is practically insoluble in water, and only slightly soluble in many of the volatile solvents. When heated rapidly it gradually darkens and decomposes at 185.5° C.

7. Sodium-2-hydroxymercuri-6-chlorthymolate.—A sample of thymol-2-(hydroxymercuri)-6-chlor-oxide was warmed with a 5 per cent sodium hydroxide solution to effect cleavage of the oxide linkage and formation of sodium hydroxymercuri chlorthymolate. Prolonged warming

failed to completely dissolve the compound. The mixture was filtered while warm and the filtrate allowed to evaporate spontaneously. A discolored crystalline compound was obtained which when recrystallized from water yielded slender, white needles. This compound was extremely soluble in water giving a clear, colorless solution. After standing a few days the needles fall into a white powder as if efflorescence had occurred, and upon longer standing the compound undergoes further change, finally becoming practically insoluble in water.

DISCUSSION.

In the formation of the acetoxymercuri derivatives of both nitrosothymol and chlorthymol, alcohol has been used as the solvent in the reactions because it appeared to be the best mutual solvent for the mercuric acetate and the substituted thymol being mercurated, and also because there was a marked difference in the solubility of the resulting mercury derivative in hot and cold alcohol. There is, however, one disadvantage in the use of alcohol as a solvent, since upon long continued boiling some of the alcohol apparently is oxidized at the expense of the mercuric acetate. This accounts for the appearance of mercurous acetate as an undesirable impurity in the mercurated derivatives. This is most easily removed by dissolving the product in weak alkali solution, forming the soluble sodium hydroxymercuri thymolate, and leaving a residue of mercurous oxide which is removed by filtration. The thymolate can then be reconverted to the desired type of derivative by pouring into a solution of a salt or acid containing the appropriate negative radical.

The substitution of the acetoxymercuri group in 6-chlorthymol is evidently in position 2. This is established by the fact that upon replacement of the mercury group with iodine, and oxidation of the resulting iodo-6-chlorthymol, a substance was obtained which was identified as 2-iodothymoquinone. To further substantiate this view, the 2-iodothymoquinone, upon being converted into the corresponding oxime or isonitroso derivative, gave a compound having a melting point identical with that reported for 2-iodo-6-nitrosothymol, the compound tautomeric with 2-iodo-6-isonitrosothymoquinone. Since in turn the chlormercuri, brommercuri, the sodium hydroxymercuri thymolate and the oxide derivatives of chlorthymol were all obtained directly from the 2-acetoxymercuri-6-chlorthymol, it must follow that the mercury group in all of these derivatives occupies position 2. Just as in the corresponding mercurated nitrosothymol derivatives previously described only mono-mercurated derivatives of chlorthymol were obtained.

SUMMARY.

(1) 6-Chlorthymol was mercurated to yield 2-acetoxymercuri-6-chlorthymol.

(2) The acetoxymercuri derivative in turn yielded 2-chromercuri-6-chlorthymol, 2-brommercuri-6-chlorthymol and thymol-2-(hydroxymercuri)-6-chloroxide.

(3) The oxide yielded sodium-2-hydroxymercuri-6-chlorthymolate.

(4) The position of the mercury group in each of these compounds was proved by replacing the mercury with iodine and oxidizing the resulting product to 2-iodothymoquinone. The latter in turn was used to obtain 2-iodo-6-isonitrosothymoquinone.

REFERENCES.

(1) Bordeianu, C. V., *Arch. Pharm.*, 272, 8 (1934), through *chem. Zentr.* (I) 2123 (1934).
(2) Kehrmann, Fr., *Ber.*, 22, 3266 (1889).
(3) Kamm, O., *Qualitative Organic Analysis*, 2nd Edition, 172 (1932).
(4) Kehrmann, Fr., *J. prak. Chem.*, (2) 39, 395 (1889).

A PHYTO-CHEMICAL STUDY OF IRIDÆA LAMINARIOIDES.*

BY JOHN ALAN ELLEGOOD.[1]

INTRODUCTION.

Seaweeds have been used for food since ancient times. In Japan to-day algæ of different varieties constitute an important factor in the dietary. Some varieties are cultivated as a crop and as such are harvested. However, the bulk of the supply is collected from natural sources. The demand is not attributed so much to the food value, which is extremely low, but to the flavor and consistency imparted to foods. Considerable work has been done on the vitamin content of seaweeds, some of which have been found to contain varying large amounts of Vitamins B and C. (1). Many of the Japanese soups are flavored with "Nori" a green alga Ulva lactuca. In American markets may be found "Dulse," (Rhodymenia palmata) one of the red algæ. "Dulse" is gathered from the coast of Newfoundland, dried and packaged for sale. It is used as a pudding thickener and as a source of iodine. A candy has been made from the stipe of the giant kelp, Nereocystis Lutkeana, also "seatron," a substitute for preservation citron, (2) from the same source.

Attempts have been made from time to time to utilize seaweed as a stock food but with little success. It has been used by coast farmers to fertilize their land (3). Besides the aforementioned uses, seaweeds have a more important place in our lives. In Pharmacy, products obtained from algæ are extensively used. Chondrus Crispus and the Mucilage of Chondrus appear in the National Formulary VI. Fucus was official in the fifth edition but has been dropped from the sixth. Agar is included in the Pharmacopœia. Agar has so many uses and is so well known that a description here would be superfluous.

Since the greater part of the agar on the market is imported, it seemed desirable to determine if a substance similar in nature could be prepared from some of the native seaweeds, of which there is a great abundance.

With this in view, Red, Green and Brown algæ were collected[2] at the University of Washington Oceanographic Laboratory at Friday Harbor, Washington. Due to the vast amount of material available, collection was limited to those varieties which occurred abundantly and those whose thalli were comparatively large and simple in form. Twenty-three were finally selected for the preliminary work.

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[1] This work was supervised by H. A. Langenhan, Professor of Pharmacy.

[2] Under the supervision of Dr. George B. Rigg, Professor of Botany.

Table I lists the species collected, the last column indicating whether gel forming constituents were found.

TABLE I. (4)

Family Species.	Description.	Results.
Green		
Ulva lactuca	Thin sheets	Non-gelling
Ulva latissima	Thin sheets	Non-gelling
Brown		
Costaria costata	Thick broad fronds, heavy round stipe	Non-gelling
Cytosiphon	Small, tubular	Non-gelling
Nereocystis lutkeana	Very large kelp	Non-gelling
Hedophyllum	Broad, crinkled, short stipe	Non-gelling
Laminaria saccharina	Broad, smooth	Non-gelling
Laminaria bullata	Broad, crinkled in the center	Non-gelling
Red		
Iridæa laminarioides	Broad form with undulating edge	Gelling
Porphyra naiadum	Very thin, edges wavy, a broad form	Non-gelling
Turnerella pacifica	Variable size, margin much lobed	Gelling
Prionitis (three varieties)	Small, much branched	Gelling
Gigartina papillata	Medium size, covered with spines	Gelling
Rhodymenia pertusa	Very long, 4′–5′; many nodules and perforations	Non-gelling
Agardhiella coulteri	Small form, much branched	Gelling
Polyneura latissima	Small, pleated thallus, toothed margin, veined	Non-gelling
Fauchea fryeana	Bladelike, small	Non-gelling
Anatheca	Somewhat dichotomously branched	Gelling
Nitophyllum mirabile	Membraneous, deeply lobed	Non-gelling
Opuntiella californica	Flat, disk-shaped frond	Gelling
Dasyopsis plumosa	Finely branched, small type	Gelling
Callophyllis	Medium size, lobed	Non-gelling
Constantinea subulifera	Circular frond, leathery texture	Non-gelling

Iridæa laminarioides was selected for the first detailed study, as it is fairly abundant and the thalli are large and unbranched thus facilitating the cleaning and drying of the large amount required for this work.

The original method employed in the preparation of a gel was that used commercially in the preparation of agar (5). It consists briefly of boiling the bleached seaweed in a large excess of water for about eight hours. It is then expressed through muslin and the residue again boiled for another period of eight hours. In this second extraction, sulfuric acid is added to about 0.5%. Practically all of the plant is dissolved, leaving very little to strain out. Later this method was modified to the extent that the sulfuric acid was omitted as it was found that partial hydrolysis took place thus decreasing the yield of the gel.

After straining, the extract is reduced to a thick gel. This must be thick enough to retain its shape when cooled. The gel is then frozen solid and allowed to melt quite rapidly, allowing the water to run off and carrying with it the water soluble portion. The residue is then completely dried and is ready for use.

Each of the specimens listed in Table I were treated in the same manner. Many were found that would produce a good gel (see Table I), however, the thallus was either too finely branched to handle well or the whole plant was so small that it would have been quite impracticable to collect for commercial purposes.

OCCURRENCE.

Iridæa is reported as being found on the Pacific Coast from Santa Barbara northward (6). Agardh reports it off the coast of Peru, and later investigators place its habitat farther south in the cooler waters of Chile (7). Iridæa edulis, also known as Dilsea edulis and Schizymenia edulis is common around the British Isles (8). Still another variety is Iridæa mertensiana which occurs

in Japan (9). The species used in the present investigation was collected in Puget Sound in the vicinity of the Oceanographic Laboratory of the University at Friday Harbor, Washington. This alga appears to be fairly common in the cooler latitudes; however, it has not been reported growing on the Atlantic coast.

Iridæa laminarioides is a member of the red algæ (Rhodophyceæ). Family, Gigartinaceæ. According to Kylin it is identical with I. heterocarpa (10). It grows attached to rocks in the upper sublittoral zone, being exposed only at extremely low tides. All of the specimens found were growing in areas where swift tide currents prevailed. There are cystocarpic and tetrasporic plants, indicating the alternation of generation common to red algæ. It is not known whether Iridæa is annual or perennial.

DESCRIPTION.

The thallus of Iridæa is short and broad and usually has an undulating margin. The stipe is extremely short, rounding out to form a modified disk-shaped holdfast. The color ranges from a deep maroon through purplish red to cinnamon-brown. In older plants and those that have been subjected to extended desiccation bleached patches will be found. These patches are very fragile and fall to pieces with handling. When submerged Iridæa is very iridescent. This property is retained through desiccation, bleaching and subsequent immersion.

COLLECTION OF MATERIAL.

The material for this work was collected from a group of rocks lying off Brown's Island across the bay from the Laboratory. The plants were accessible only during minus tides making collection somewhat delayed. Approximately two gunny sacks of air-dried material was collected. The actual collecting was done from rowboats, the material being pulled from the rocks and placed in tubs of salt water. On returning to the station, the plants were stored in live-boxes until such time as they could be worked upon, which was never more than twenty-four hours after collection. Cleaning consisted of going over each thallus by hand to remove the larger adhering foreign material. They were then washed in running sea water followed by fresh water. Long strips of muslin were placed in the sun and the cleaned seaweed spread upon this. After it had dried, it was collected, macerated in fresh water and returned to the muslin strips. This was repeated until the thalli were bleached to a pale straw color. The bleached Iridæa was then dried and stored in tightly closed manila bags.

ANALYTICAL DATA.

Moisture.—The moisture of the fresh thallus was determined by first removing the surface water with dry cloths and then drying to constant weight at 100° C. Moisture content—89.47%.

Ash.—The methods used for determining ash and its constituents were those of the A. O. A. C. (11). Samples were run in duplicate and repeated for accuracy. All determinations were based on material dried to constant weight at 100° C.

Total ash	16.08%
Insoluble	3.27%
Soluble	12.81%
Ca	0.391
Na	0.53%
K	2.34%
SO_4	3.52%
Cl	1 54%
P_2O_5	0 7373%

Iodine.—Considerable difficulty was experienced in obtaining a suitable method for the determination of iodine. The colorimetric method of Tang and Whang (12) was attempted, but the results were not consistent. McKean (13) developed a method based on the extraction of the sample with water. This method would not apply to Iridæa as the plant swells and becomes very viscous in water and is impossible to filter. The U. S. P. method for Thyroid could not be used because of the very small amount of iodine present. The smallest trace of chlorine would give a very high iodine value. The following method was found to give 96.26% recovery of added iodine (as KI) to agar. It is essentially the method for the assay of Thymol Iodide U. S. P. XI.

The material is ignited to a dull red with anhydrous sodium carbonate. When it is thoroughly charred, it is washed onto a filter paper and the whole mass washed with about 150 cc. of hot distilled water. Enough solution of potassium permanganate is added to produce a pink color. Ethyl alcohol is added to reduce the excess permanganate and the solution made to 2,000 cc. with water. This is then filtered, the first 25 to 50 cc. being discarded and a 100-cc. aliquot taken for titration. KI and dilute H_2SO_4 are added to the aliquot which is then titrated with 0.001 normal sodium thiosulfate. In standardizing the method blanks were run on the reagents, on agar and on agar plus a measured amount of KI. To determine the recovery, exactly 1 Gm. of KI was diluted to 100 cc. and one cc. of this, representing 0.01 Gm. was added to two Gm. of agar. Simultaneously the blanks were run. After deducting the titration values of the blanks, it was found that of the 0.00764 Gm. of iodine added (as KI), 0.007354 Gm. were recovered. Following the above procedure Iridæa was found to contain 24.32 parts per million of iodine.

Nitrogen.—The method used was the Kjeldahl-Gunning Arnold method (14). Duplicates were run along with a blank of the reagents used. The results: Iridæa 1. 3.23% nitrogen.

EXTRACTIVES.

Selective Solvents.—A series of extractions were made using a soxhlet extractor and extracting for a period of eighteen hours.

Table II gives the results of the extraction. In each case the residue left after the evaporation of the solvent was a very thin greasy film on the bottom of the soxhlet flask. The amounts were so small that it was not considered feasible to attempt an analysis.

TABLE II.—SEPARATE SAMPLES FOR EACH SOLVENT.

Solvent.	Per Cent of Extract.
Ethyl ether	0.24
Chloroform	0.21
Petroleum ether	0.19
Alcohol	0.70

Fractional Extraction.—Another set of extractions was made using petroleum ether, chloroform, ethyl ether, ethyl alcohol and water, in the above order.

TABLE III.—ONE SAMPLE EXTRACTED SUCCESSIVELY.

Solvent.	Per Cent of Extract.
Petroleum ether	0.1968
Chloroform	0.1937
Ethyl ether	0.2050
Ethyl alcohol	0.4530
Water	86.34

Qualitative Tests.—An alcoholic extraction was made of a comparatively large amount of the material. Following the method of Hassid (15), the alcoholic solution was filtered and reduced in volume until a syrup consistency was obtained. This was allowed to stand for several days when a few crystals were obtained. These were redissolved in a very small amount of alcohol and allowed to recrystallize. The melting point of the crystals was 183° C., agreeing with the melting point for dulcitol. The few remaining crystals were hydrolyzed with nitric acid to mucic acid. This was checked by the melting point. From this it was assumed that dulcitol was obtained from the alcoholic extract.

Both aqueous and alcoholic extracts responded to the following tests.

Carbohydrate	Molisch test	Positive
Reducing sugars	Benedict's	Negative
	Fehling's	Negative
Pentosan	Phloroglucinol-HCl	Negative
Galactan	Mucic acid	Positive

Crude Fiber.—Following the method as outlined in the A. O. A. C. (16). Crude fiber was determined on Iridæa laminarioides with the following results: Crude fiber 0.705%.

PHARMACEUTICAL.

An attempt was made to substitute the extract obtained from Iridæa laminarioides for some of the gels and gums used in official preparations.

As a preliminary step various dilutions of tragacanth were made and these compared with similar dilutions of the Iridæa extract by the falling ball method of Nicholls (17). It was found that an aqueous dilution of 1:40 of Iridæa compared with an aqueous dilution of 1:100 of tragacanth.

The following preparations were made substituting the extract for the tragacanth; glycerite of tragacanth; jelly of ephedrine sulfate; and an emulsion of olive oil (18).

In each case the product was not as attractive as that in which tragacanth was used. The color resembled agar products. The consistency was similar if about $2^1/_2$ times as much Iridæa extract was used in the place of tragacanth. Emulsions made with the extract tend to separate more readily than those made with tragacanth or acacia.

SUMMARY.

A survey was conducted on various Red, Brown and Green algæ to determine their gelling properties. Iridæa laminarioides was chosen as the first upon which to make a detailed study. The chemical constituents were determined, and a comparative pharmaceutical study of the aqueous extract was made. For one part of tragacanth $2^1/_2$ parts of Iridæa extract are required in order to obtain a product of comparable consistency.

BIBLIOGRAPHY.

(1) Norris, E. R., *J. of Nutrition*, 13, 4 (April 1937).

(2) Tilden, A., *Algæ and Their Life Relations*, Univ. of Minnesota (1925).

(3) Gray, S. O., *British Seaweeds*, L. Reeve & Co., London (1904).

(4) Kylin, H., *Marine Red Algæ in the Vicinity of Friday Harbor, Washington*. Harrowitz, Leipzig (1928).

(5) Tressler, D. K., *Marine Products of Commerce*, Chemical Catalog Co., New York City (1926).

(6) Hervey, A. B., *Sea Mosses*, Orange Judd Co., New York (1895).

(7) Howe, M. A., *Algæ of Peru*, New Era Press, Lancaster (1910).

(8) Newton, L., *Handbook of British Seaweeds*, Trustees of the British Museum, London (1933).

(9) Okamura, K., *Icones of Japanese Algæ*, 3, 83 (1913–1915).

(10) Kylin, H., *Marine Red Algæ in the Vicinity of Friday Harbor, Washington*. Harrowitz, Leipzig (1928).

(11) *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 4th Ed., XII, 4, 10, 14, 15, 28, 36, 30 (1933).

(12) Tang, Pei-Sun, and Whang, Pao-chun, *Chinese J. Physiol*, 9, 285–289 (May 1935).

(13) McKean, J. B., *The Analyst*, 61, 11 (January 1936).

(14) *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 4th Ed., II, 22 (1933).

(15) Hassid, W. Z., *Plant Physiology*, 8, 480 (July 1933).

(16) *Official and Tentative Methods of Analysis of the Association of Official Agricultural Chemists*, 4th Ed., XII, 52 (1933).

(17) Nichols, A. B., Jour A. Ph. A., 26, 823 (1937).

(18) *Pharmacopœia of the United States*, 11th Revision, Mack Printing Co., Easton, Pa. (1936).

VISCOSITY "FLOW TIME" TEST.*

BY BERNARD FANTUS AND H. A. DYNIEWICZ.

There is need, it seems, for a simple viscosity test that can be performed by any pharmacist with inexpensive and readily available equipment. The difficulty experienced in securing uniformity in the official Ephedrine Jelly is illustrative of this need. Various specimens of tragacanth differ in their jelly-producing power to so great an extent that indicating the percentage of tragacanth which a preparation should contain by no means ensures the proper degree of consistency. What we need is to specify the quantity of "standard tragacanth" or other gel-producing colloid and the consistency aimed at; and to permit the pharmacist the determination of the actual quantity of the colloid he has that is required to secure the result aimed at.

As Middleton[1] and others[2] have shown "The viscosity of such colloidal sols and gels as tragacanth mucilage does not show true viscosity independent of rate of flow, but has the property of 'anomalous' or 'variable' viscosity, *i. e.*, the ratio between applied pressure (rate of shear) and rate of flow is not constant, but decreases rapidly as the rate of shear increases. It is, therefore, impossible to express the viscosity of a tragacanth mucilage by any single figure, but the conditions under which it has been determined must also be specified."

We believe we have elaborated a method so easily performed and with so simple an equipment that it may deserve to be better known. The principle underlying the test is the measurement of the "Flow Time," *i. e.*, the time elapsing until the jelly has come to rest at a certain level; and measuring the angle this level assumes with the vertical and the time within which this level is assumed. With this method constant conditions are readily maintained as the rate of shear is practically constant.

"FLOW TIME" TEST.

Square-cornered bottles (4-ounce size) with screw tops (Fig. 1)[3] should have a mark at the point to which 60 cc. of contents come. The bottle is filled to this point with the jelly that must have been homogenized and permitted to attain a specified temperature, *e. g.*, room temperature (25° C.). The bottle is then placed upon its side and a stop-watch started at this moment.

The test requires recognition of three types of jelly: (*a*) "horizontal" jelly; (*b*) "angle" jelly; and (*c*) "vertical" jelly.

A. Horizontal Jellies.—If the jelly is thin enough to assume the horizontal or practically horizontal level, *i. e.*, that has made an excursion of 90° within an hour after the bottle has been laid on its side, we may speak of a "horizontal" jelly. The first observation is discarded, and subsequent observations are made in such a way that the same side of the bottle is always down. The bottle is then placed upright and permitted to stand thus as long as it took to acquire the level of equilibrium. A sufficient number of tests is then made to secure a fair degree of uniformity in the time intervals, and these are averaged and reported, *e. g.*, Flow Time = 90° in 1 sec., or Flow Time = 90° in 7 min., etc.

B. Angle Jellies.—With denser jellies, when the horizontal level is not reached within an hour, the observation is ended at this time and the angle of deviation from the vertical is noted.

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* From the Laboratory of Pharmacology and Therapeutics, University of Illinois, College of Medicine; and assisted by a grant from the AMERICAN PHARMACEUTICAL ASSOCIATION.

[1] Middleton, G., YEAR BOOK PHARM., 9, 491 (1936).

[2] Brindle, H., and Brown, J. M., *Ibid.*, page 161.

[3] One hundred twenty cubic centimeters (4 oz.), square wide-mouth bottle, screw top. Sargent's S9195.

Thus, when the surface of the jelly has traveled within the hour to 45°, it is recorded as: Flow Time = 45° in 1 hour.

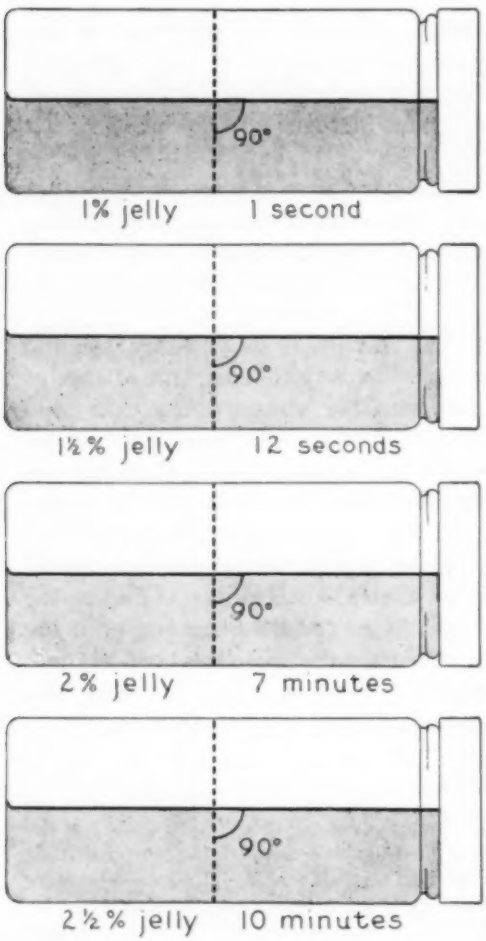

Chart I.—"Horizontal" jellies. "Flow Time."

C. Vertical Jelly is the term we propose to be applied to those gels the surface of which has not moved, *i. e.*, remained vertical by the end of the hour's observation period during this test. If the vertical level of the surface is unchanged at the end of the hour, we speak of a 0° or a vertical jelly which is recorded as: Flow Time = 0° in 1 hour.

To determine the least amount of tragacanth required to prepare a vertical jelly with a particular quality of tragacanth, a fresh jelly with reduced quantity of tragacanth needs to be prepared in these tests as *e. g.*, a 50% dilution of the prepared jelly gives a different result from a

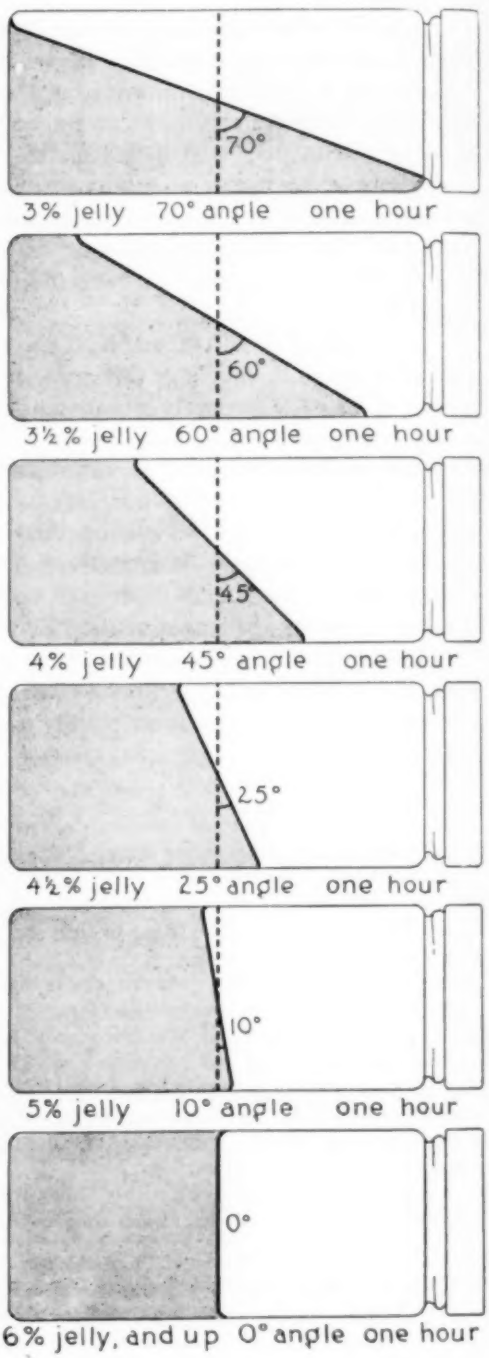

Chart II.—"Angle" jellies, 1 hour "Flow Time."

freshly prepared jelly with one-half the quantity of tragacanth employed. The denser the jelly and the greater the degree of dilution the more erratic is the result.

By means of this test not only is it possible to distinguish between the colloidality of different qualities of tragacanth, but also to detect adulteration of tragacanth with less jellyfying material.

To prevent pellicle formation, all observations with a certain jelly should be made within a few hours.

Table I illustrates the method of recording of the result actually secured with a certain quality of tragacanth, as well as the fact that this test is capable of distinguishing between increments of ½% in strength between certain limits.

TABLE I.—"FLOW TIME" TEST FOR A CERTAIN RIBBON TRAGACANTH.

(Cf. Chart I and II.)

1%	=	90° in 1 second
1½%	=	90° in 12 seconds
2%	=	90° in 7 minutes
2½%	=	90° in 10 minutes
3%	=	70° in 1 hour
3½%	=	60° in 1 hour
4%	=	45° in 1 hour
4½%	=	25° in 1 hour
5%	=	10° in 1 hour
6%	=	0° in 1 hour

Jellies, like gelatin, that have a higher melting point than room temperature are tested at a uniform temperature that secures proper consistency for flow time measurement and the temperature statement is included in the report, *e. g.*, Flow Time = 90° in 7 min. at 37° C.

OFFICIAL SPECIFICATIONS FOR FLOW TIME TEST.

Should this test be found acceptable by our official formularies, some such specifications as the following might be proposed to be included in the monograph, *e. g.*, the one on tragacanth.

"Standard tragacanth should have the following jelly-producing quality: 4% of the tragacanth made into a jelly in accordance with specifications under test for identity and purity should yield a jelly that has a flow time test of 45° in 1 hour (or not less than 40° nor more than 50°)." Specimens having other flow time test require, to be official, a statement of the deviation from the standard.

Commercial specimens of tragacanth should bear the declaration of the relation of this tragacanth to the standard official tragacanth so that the pharmacist may know the relation of the quantity of this specimen to the tragacanth of official quality, he may have to use to secure approximately equal consistency.

CONCLUSIONS.

1. We find a simple flow time test a fairly accurate means of standardizing the consistency of jellies and of determining the percentage of tragacanth or of other gel-producing colloid contained in a jelly.

2. In consequence the jellyfying qualities of different colloids may be compared with each other.

3. The flow time test makes it possible to lay down official standards for tragacanth and other colloids.

4. This test makes possible to determine the effect of chemical and other influences upon tragacanth and other jellies.

APPLIED PRINCIPLES OF PROFESSIONAL PHARMACY.*

BY MAX N. LEMBERGER.[1]

Many papers have been read before state and national organizations and numerous articles have been published in professional journals on Pharmacy and the relationship between pharmacist and physician. After careful study of these, many questions naturally present themselves. The most frequent thought is probably, "What is a professional pharmacy?"

A professional pharmacy, as has been variously stated, is that type of pharmacy in which 60 per cent of the volume consists of prescriptions and drug sales, an establishment that promotes a more intimate contact and feeling of interdependence between physician, dentist and pharmacist. It is well to mention here that one must bear in mind that the major support of a professional pharmacy must come from the medical and allied professions.

A professional store can never straddle the fence by attempting to solicit the support of the physician while entering into competition with him by counter prescribing. As pharmacists, we are equipped to prepare medicinal preparations but not to diagnose and practice Medicine.

When the professions coöperate, the pharmacist comes into his true functioning power as an important helper and both physician, dentist and pharmacist are in better position to render an invaluable service to the community. The professional pharmacy offers a trained pharmacist dignified employment and full opportunity to develop his capabilities.

The professional pharmacist realizes the responsibility placed upon him in preparing, compounding and dispensing medicinal products. The commercial aspect is secondary and the honest desire to carry on as a professional man inspires him in his undertaking. His knowledge of the purity and quality of the products dispensed is important both to the physician and to the welfare of the patient. The pharmacist's familiarity with modern remedies, specialties of pharmaceutical manufacturers, the variety of synthetic chemicals and biological products, and his fundamental acquaintance with scientific research, methods of standardization, storage and handling delicate and complex compounds are wonderful factors in establishing complete confidence between pharmacist, allied professions and patient.

The professional pharmacist must continue his studies after leaving college; he finds it helpful to attend pharmaceutical, chemical and allied educational meetings. He must keep abreast of all current professional literature and consequently must maintain a complete file of it and an up-to-date library for quick reference in order to fulfil such specialized demands as are made upon him from time to time.

The stock of a professional pharmacy must be keyed to the prescribing habits of local physicians. It should consist of the newer specialties, vitamin products, allergenic extracts, biologicals, ampuls, chemicals and the usual tinctures and fluid-extracts of the U. S. P. and N. F. sick-room accessories, clinical laboratory,

* Presented before the Section on Practical Pharmacy and Dispensing, A. PH. A., Minneapolis meeting, 1938.

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equipment and glassware, reagents and stains. With the recognition by the N. F. VI of the importance of these reagents and stains, the pharmacist has reliable authority under which to seek this type of business.

Equipment should be extensive; analytical balance, torsion balance, chemical glassware, beakers, flasks, pipettes and burettes, refrigerator for storage of biologicals and autoclave for preparing special ampul medication and sterile dressings. Many other pieces of equipment might be mentioned which from our experience have been proved to be essential; however, I mention these few to bring my thought of needed equipment to a better and clearer picture.

Personality and individuality are important. Identification of the pharmacy is likewise worthy of much thought and I know of no better expression and advertising than the packaging of prescription products of liquid nature in carton enclosures, and the adoption of distinctively designed boxes and labels. These are silent advertisers and reflect the character of the proprietor, and indicate interest and painstaking precision in prescription preparing.

This all may seem elementary and appear as repetition of dissertations previously read and heard at pharmaceutical conventions and meetings; however, before a presentation of some of the applied practices of professional pharmacy can be given one must first have a clear picture of the type of pharmacies to which these practices are applicable. Therefore with this thought in mind, having first covered this subject in a general manner, I shall endeavor to cover separately some of the most important practices that have proved profitable in their application.

Library and Literature File.—The library should be as extensive as finances permit. Standard reference books, required by law in most states, such as U. S. P. XI, N. F. VI, U. S. Dispensatory, New and Nonofficial Remedies, Remington's Practice of Pharmacy, Pharmaceutical Recipe Book, A. PH. A. YEAR BOOKS, Gutman's Encyclopedia of Drugs, Accepted Dental Remedies, Todd and Sanford's Laboratory Methods, Merck's Index and Manual, are all indispensable. The physician soon realizes that any references needed in his practice are available and obtained more conveniently at your store than at the medical library, with a saving of much time.

A literature file in a few years' time will consist of thousands of pieces of descriptive material of specialty products, house organs of pharmaceutical manufacturers' clippings from various medical journals and the *American Medical Association Journal*. Many physicians do not subscribe to this journal because they limit themselves to a particular specialized field of Medicine and feel that journals published covering their special field are ample, but will, however, occasionally hear about some article appearing in the *American Medical Association Journal* and then will interest themselves in the particular journal, and yet are prone to ask fellow practitioners. The AMERICAN PHARMACEUTICAL ASSOCIATION JOURNAL and YEAR BOOK are used equally as much for valuable data, as these books in abstract form usually give the information desired. All of this type of material should bear a rubber stamp stating "from the Library" using the pharmacy's name or title by which known in the community. When more than one piece of the enumerated references are available from your files stamp same with "compliments of," again using the store name, in addition suggesting they file same for

themselves for future reference. All journals should be kept for the current and preceding year, keeping the index numbers for a period of five years or more.

Stock.—Before placing any items on the shelves, a general knowledge of their uses should first be obtained. All efforts should be made to have a round table discussion at regular intervals with all pharmacists employed, so that all will have equal knowledge of any product available for prescription dispensing. Each item should be marked with the date of placing in stock, net cost, physicians' cost and retail selling price. The dating of items promotes excellent stock control and facilitates elimination of slow-moving specialties. One can use his own judgment as to length of time before dropping from inventory. I find a three-month period very practical.

Biological products must be thoroughly understood by every employee, and each package in addition to above marking, can be stamped "reorder from," again using store name. At regular intervals this stock should be checked to avoid stocking of outdated biologicals. Encourage the writing of prescriptions for biological products whether therapeutic or prophylactic, protein extracts, pollen treatment sets and ampul medication; in this manner the patient's appreciation for the individualized service and care the physician renders is greatly enhanced.

Equipment.—This equipment might be classified as the tools of the trade. A mechanic is usually judged by the tools he possesses and the manner and familiarity with which he uses them, so also should the pharmacist be proud to possess the necessary equipment. No greater impression is created with the physician and patient, no greater advertising medium is available than the knowledge and confidence invested in these persons you serve, that you can properly prepare the products demanded in present-day practice. Not only for prescription practice is this expected but also in the preparation of special products such as dilution of Old Tuberculin for the Mantoux test, B. E. Tuberculin for therapeutic use, pollen dilution in various dilutions for treatment, daily pollen counting of pollens prevailing in your city during the principal hay fever season, vanishing creams and protective creams for industrial institutions to mitigate certain skin conditions that may be classed as industrial or occupational, and clinical laboratory for the medical profession to assist in diagnosis of disease.

Other practices which can be put into operation, follow.

Do not permit detailing on your premises, as most physicians prefer an occasional chat other than business, or enjoy a smoke and are likely to use your store for this purpose. This is particularly true of those in office or medical buildings.

Do not hesitate having your dispensing room open for inspection by the physician and the public at any time.

Do not counter prescribe.

Do not discuss the prescription with the patient.

Do not guess at prescription prices; calculate them by using some uniform prescription-pricing schedule.

Do not hesitate to coöperate with the physician when he has in mind improving or preparing some pet medication, or assist him with a compounded preparation that may be primarily experimental.

Do not use medical terms when discussing products with the physician; use pharmaceutical terms.

Do not yourself, or permit your assistants to conduct themselves in any such manner so that professional atmosphere will be destroyed, or reflect on the professional integrity of the store.

In conclusion may I state that each of these practices has been found practical in its application and am confident can readily be applied in any professional pharmacy whose practices should whole-heartedly and sincerely engross a professional atmosphere. The professional pharmacy of to-day has a great responsibility in the program of public health service. With the endorsement of the medical profession, patronage of the public and recognition by the pharmaceutical societies, this type of pharmacy will become more and more recognized as a preferable outlet of pharmaceutical service.

CALCIUM LINOLENATE.*

BY KATHRYN GLENNON.[1]

Since the work of G. O. and M. M. Burr, at the University of Minnesota, which clearly discloses that some fats contain indispensable unsaturated fatty acids called Vitamin F, and that linseed oil and lard are characterized by varying yet large amounts of the Vitamin F ingredient, it seemed possible that an entirely new concept could be reached in a better understanding of the pharmacologic action of official lard and official linseed oil used as bases in ointment, liniment and the like.

It will be recalled that they conclusively demonstrated that animals reared on diets free from indispensable unsaturated fatty acids developed typical lesions of the skin which amounted to a dryness and roughness eventuating in eczema; and that the hair and nails similarly suffered dryness, roughness, brittleness and other changes suggesting atrophic disorders. Also, it will be recalled that the administration of exceedingly small amounts of indispensable unsaturated fatty acids, or Vitamin F, could either prevent or cure the lesions in rats subjected to this type of diet.

Lard has been an official ointment base for many years, and a review of the dermatologic literature reveals that much of the standard medication used in the external treatment of certain eczemas has remained the same for the past fifteen or twenty years, excepting that the base, generally lard, has been displaced with petrolatum or one of its many equivalents. Similarly, it would appear that the report of two decades ago clearly suggested far more favorable response to the earlier ointments than is now recorded for the present-day ointment; and since the medication has remained the same, it would seem, in the light of the discovery of the Burrs, that the lessened efficiency of the treatment might probably be ascribed to the change in the ointment base.

With these considerations in mind Dr. Weinstein and I prepared an ointment which had for its principle the blending of the natural lipids of the skin in-

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cluding lecithin and cholesterol in a base of lard, reënforced with Vitamin F or unsaturated fatty acids. The clinical effectiveness of this ointment has been separately reported and amounts to a complete corroboration of the work of the Burrs with respect to the human. In other words, many conditions which the Burrs have found to be the result of Vitamin F deficiency in the experimental animal and which seemingly have a counterpart in the human have responded to the topical application of an ointment compounded essentially of the skin lipids with accentuated reënforcement of the Vitamin F ingredient.

It will be observed that topical application was effective in these human cases, thus disposing of the question as to whether or not externally applied vitamin preparations can be effective. It can now be said with complete clinical assurance that conditions resembling Vitamin F deficiency may yield to the external application of Vitamin F applied to the skin in the form of a suitable ointment This is not an indication that all vitamins applied externally will be effective, since all vitamins have comparatively minor parts to play in skin function. But the withdrawal of Vitamin F from the diet of the animal produces typical skin lesions of an eczematous nature which unquestionably yield to the external application of highly enriched Vitamin F ointments. In this sense Vitamin F certainly is deserving of the designation "the skin vitamin," in the same sense that Vitamin D is called "the sunshine vitamin."

Whereas the effectiveness of Vitamin F ointment locally applied is seemingly unquestionable, from the standpoint of the pharmacist there is a compounding difficulty that requires study and correction. Lard, as is commonly well known, is subject to rancidity. The addition of unsaturated fatty acids to lard may in a number of instances foster this rancidity. A rancid ointment does not always result from the incorporation of Vitamin F in lard, but when it does, the ointment may become an actual irritant particularly if used on the tender skin of the infant.

The use of oils, such as linseed oil, for the purpose of securing Vitamin F in its natural state is considerably limited by the fact that in order to obtain sufficient concentration of Vitamin F in the ointment it is frequently necessary to exceed 60% or 70% level in the form of oil; and ointments containing 60% to 70% of oil are naturally fluid and unsuitable for common use by reason of their undesirable consistency; hence, the desirability of procuring Vitamin F in concentrated form.

Many esters of Vitamin F have been prepared, as for example the methyl ester, the ethyl ester and others. Not all of these esters are equally effective, and some can be considerably dangerous. It is commonly well known that the methyl derivative of many products, such as methyl alcohol, are quite toxic. They are unsafe for extended clinical use and should not be selected if they can be replaced by non-toxic effective compounds.

The esters of the fatty acids have been ushered into use largely by reason of the belief that their form permitted absorption as suggested by their solubility. However, a common experience indicated that perhaps the calcium salt of the linseed oil fatty acids could also be quite effective particularly in the treatment of first and second degree burns. Obviously, this indication is implied by the effectiveness of Carron Oil, or Lime Liniment, which is a mixture of linseed oil and lime water and produces a calcium soap which partially emulsifies the oil. Certainly, the water and the oily glycerides are nothing to commend in the treatment of burns;

and if there is any specific effectiveness in the use of Carron Oil, it seems possible that it might be linked with the calcium salt of the Vitamin F component of the oil.

It is not difficult to prepare the calcium salt of the effective unsaturates. The exact indentity of the unsaturated fatty acids responsible for the Vitamin F effect is not known. It is merely assumed that they belong to the linoleic, or to the linolenic, or probably to both groups of unsaturated fatty acids. It may be an isomer of either linoleic or linolenic or it may be one of the isomeric form of either linoleic or linolenic acids. Thus, the common statement that because linoleic acid is probably widespread in natural foods and, therefore, a Vitamin F deficiency is not likely to exist, is completely indefensible on the ground of scientific data. Since the exact nature of Vitamin F is not known, and the exact distribution of that particular compound is also unknown, such statements are entirely unwarranted and are calculated simply to mislead rather than to clarify the topic under investigation. However, for purposes of brevity, we shall designate the calcium salts that are known biologically to be effective under the generic title of Calcium Linolenate, it being understood that by calcium linolenate we are not referring to a specific chemical compound but to a mixture representing the calcium salt of the indispensable unsaturated fatty acid—or the calcium salt of Vitamin F.

The neutralization of Vitamin F unsaturates prepared properly from linseed oil with calcium hydroxide is all that is required for the manufacture of the product. The product can be purified further by frequent washings with ethyl alcohol to remove all of the free acids that have not combined with the calcium. Obviously the product is not a single chemical compound but it results in a whitish powder, insoluble in water, readily incorporated in fat and fat-like material and, most important of all, it is seemingly as effective as are the unsaturated fatty acids from which the calcium salt is derived. This implies that calcium apparently seems to select the more active fatty acids, because, if this were not true, then the calcium salt should only be about half as effective as the unsaturates from which it is prepared. Since it is of equal effectiveness, it suggests that about half of the unsaturates in a mixture of such acids are effective and that the calcium combines with that particular half.

In addition to its effectiveness which is seemingly identical with the effectiveness of the unsaturates from which it is derived, calcium linolenate is apparently stable under a great variety of conditions which makes it ideally suited for incorporation in ointments, cerates, unguents, oils, creams and similar preparations for external application. The dosage level of calcium linolenate is not entirely known but seems to be effective at about from 5% to 10%. If lard is used as the base to which calcium linolenate is added, rancidity is not particularly fostered as is the case when the unsaturated fatty acids themselves are used. However, an outstanding quality of linolenate is the ability to dispense with lard and to replace lard with petrolatum. It is true that petrolatum probably does not permit of the same degree of intradermal penetration as does lard and certain other fats; but this intradermal penetration can be conferred upon petrolatum through the simultaneous addition of lanolin and lecithin. Accordingly, a suitable Vitamin F base, without rancidity, with good absorption and with the specific effect of preventing and correcting the skin disorders that arise in consequence of Vitamin F deficiency can be

compounded through the use of calcium linolenate according to a formula patterned somewhat as follows:

Calcium Linolenate	5.0
Lecithin	5.0
Anhydrous Lanolin	5.0
Petrolatum, white or yellow	85.0

An ointment compounded on this basis needs no additional medication for the correction and prevention specifically of allergic eczema—the type which apparently develops because of Vitamin F deficiency.

Not only is the ointment suggested suitable for the treatment of specific eczemas, but it lends itself admirably well for the treatment of first and second degree burns. It is, in reality, a Carron Oil in solidified form or, more properly, it is the active ingredient of Carron Oil in a proper pharmaceutic ointment base.

Calcium linolenate ointment has been used on a few occasions to displace petrolatum in the treatment of osteomyelitis, and although the reports are few, they are unanimously highly satisfactory. It appears that packings of calcium linolenate ointment as formulated above not only served the purpose of petrolatum, which comprises 85% of the ointment, but displays at the same time a bacteriostatic effect and a definite bone proliferative effect. It is well known that the unsaturated fatty acids are quite selective in their ability to destroy and inhibit the activities of certain bacteria. Apparently, calcium linolenate slowly releases the Vitamin F and makes for a long-continued activity of this slow bacteriostatic effect which is probably helpful in the treatment of osteomyelitis.

An unusual and interesting use for calcium linolenate is its incorporation in talc intended for use on the baby. From 1% to 3% of calcium linolenate mixed with talcum and perfume and intimately ground in through the use of the ball mill produces a medicated talc which seems to act with unusually splendid effect in overcoming the rashes to which the baby is subject with far greater promptness than talcum not so medicated.

A most effective use of calcium linolenate ointment is in the prevention, and better, in the treatment of erythema solaris or sunburn.

While we are not prepared to discuss the biologic activity of calcium linolenate as standardized by assay, we are sufficiently advanced in our study to suggest that calcium linolenate is most effective when prepared from unsaturates whose biologic assay in Shepherd-Linn units has been established. In other words, if the biologic activity of the unsaturates is known, the biologic activity of the calcium linolenate can be quite accurately expressed.

Calcium linolenate is a tremendously effective protective ingredient and seems to have every possibility of displacing zinc oxide. Since it is needed in only one-tenth the amount that is required of zinc oxide, a 1% calcium linolenate ointment being fully as protective as a 10% zinc oxide ointment, it follows that such ointments are much more economical for general hospital use since the unit cost of calcium linolenate is considerably less than ten times that of zinc oxide.

BIBLIOGRAPHY.

(1) Burr, G. O., and Burr, M. M., "On the Nature and Rôle of the Fatty Acids Essential in Nutrition," *J. Biol. Chem.*, 86, 587–621 (1930).

(2) Cornbleet, T., "Use of Maize Oil (Unsaturated Fatty Acids in the Treatment of Eczema)," *Arch. Derm. and Syphil.*, 31, 224–226 (1931).

(3) Burr, G. O., Burr, M. M., and Miller, E. S., "On the Fatty Acids Essential in Nutrition," *J. Biol. Chem.*, 97, 1–9 (1932).

(4) Evans, H. M., and Lepkovsky, S., "Vital Need of the Blood for Certain Unsaturated Fatty Acids," *J. Biol. Chem.*, 99, 231–234 (1932).

(5) Hansen, Arild E., "Study of Iodine Number of Serum Fatty Acids in Infantile Eczema," *Proc. Soc. Exper. Biol. Med.*, 30, 1198–1199 (1933).

(6) Hansen, A. E., "Serum Lipid Changes and Therapeutic Effects of Various Oils in Infantile Eczema," *Ibid.*, 31, 160–161 (1933).

(7) Oncken, Mildred, "Unsaturated Fatty Acids (Vitamin F) Deficiency," *Ill. Med. Jour.*, 67, 236–239 (1935).

(8) Shepherd, M. I., "Vitamin F in Skin Creams," *Drug and Cosmetic Ind.*, 12, 30 (1936).

(9) Glennon, Kathryn, "Vitamin Soaps," *Soap*, (November 1936).

(10) Weinstein, M. L., and Glennon, Kathryn, "Vitamin F Ointments," *Ill. Med. Jour.*, (June 1937).

COMMENTS OF AN EXPERIENCED HOSPITAL PHARMACIST.*

BY PAUL D. BROWN.[1]

So much has been said recently relative to the establishment, standardization and conducting of a hospital pharmacy that it would seem there is little left to be commented upon. However, to make a story more impressive it needs to be repeated over and over again. Each reading makes a new and different impression on the mind, thus helping one to obtain more useful knowledge than might be gained from a casual reading. If, in the short space allotted to this paper I may make some suggestion or even repeat some thought oft expressed, which will be of some value to a fellow member, I shall feel well repaid for my humble effort.

First we might ask what is a hospital pharmacist? The most natural answer to this question would be "one who dispenses drugs in a hospital." However, if we stop to look over the field we come to the conclusion that hospital pharmacists at present may be nurses, doctors, internes or even (though I blush to mention it) sometimes maids and janitors. It is my humble opinion that a hospital, however small, should be placed under the same restrictions, regarding the dispensing of drugs, as any drug store, and required to have a registered pharmacist in charge at all times.

The dispensing of drugs to patients in hospitals is, to my mind, an important professional duty and should be entrusted only to one who has been educated and trained for that particular purpose. The professional duties are far more complicated and extended than those of an ordinary pharmacist and I am heartily in accord with the idea of pharmaceutical interneship as is being formulated by some of our more prominent Schools of Pharmacy over the country.

The practicability or feasibility of such an interneship has been forcibly brought to the writer's attention on many occasions when after employing an assistant pharmacist who had come with the best of credentials as to character, education, ability and ambition, it became necessary to spend much time and patience in ac-

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quainting him with the special technique and routine of hospital practice. An internship would help to prepare a student for a more responsible position and to render more satisfactory service in his chosen profession.

It is my firm conviction that, in addition to the qualifications or credentials above mentioned a hospital pharmacist must be endowed with a vision, an innate desire to be of service to his fellowmen and a will to render a better service, not permitting the necessary pecuniary benefits to dominate or control his efforts.

It has been well said that "A task without a vision is drudgery" and I am led to believe that a vision of greater things to be accomplished, a love of service to humanity and a strict application of ideals are essentials in the life of a hospital pharmacist, thus enabling him to better serve the patient, doctor and hospital, and reflect credit upon the profession of Pharmacy.

In the remote past the existence of a hospital pharmacist was not always one to be coveted. For some unknown reason it had been the custom in most hospitals to relegate the pharmacy to some section of the building where the pharmacist in charge, if any, could "ply his trade" in peace and quiet.

It was usually operated as an unknown quantity so far as contact with the medical staff or other departments was concerned. It is pleasing to note, however, that under the light of a new dawn this custom is becoming obsolete and to-day we find in most hospitals, the pharmacy and the pharmacist are receiving their just and proper recognition as an essential unit of a complete hospital service. Whatever may have been the conditions regarding the hospital pharmacist previously it is to be noted with some degree of pride that since the establishment of the subsection on Hospital Pharmacy by the A. PH. A. much publicity has been given and many kind words spoken in behalf of the hitherto more-or-less forgotten man.

Much has been written and diverse opinions expressed in regard to conducting a hospital pharmacy, and I am frank to admit that some useful knowledge may be gained by carefully reading such articles as have appeared in various Journals and adopting whatever plans or suggestions may appeal to the reader and his particular situation. We must admit that each individual hospital has many problems peculiar to itself which might not apply to others. Especially is this true when considering institutions of different capacities and locations. However, there are many phases of work and routine which are common to all and differ only as relates to the volume required.

Within the writer's experience of some eighteen years it has been interesting to note the ever-changing conditions even in the same hospital, each succeeding year bringing new problems, due perhaps to the growth of the hospital, the advance in research work or to the changing cycle of medication.

One of the most important items, from a standpoint of service, is the location of the pharmacy. It is not always an easy matter to solve this problem to the satisfaction of all concerned, especially in the older institutions which were constructed when the importance and essentials of a pharmacy were of less consequence. We find in some of our modern structures that this feature has been taken care of to a marked degree not only in regard to adequate distribution of drugs and supplies to the various wards and floors, but also as a convenient location for the physician to meet the pharmacist in consultation on points of mutual interest.

In a few hospitals we note that it is becoming a custom to extend the services of the pharmacist beyond the limits of patients and physicians by supplying the little necessities of life to relatives and friends of patients who may be forced to remain in the hospital for some days. This additional service, although not necessarily professional, may be made an asset of some consequence to the hospital in proportion to the location of the hospital, the location of the pharmacy in the hospital and the type of service rendered.

Next to the location I am convinced that equipment is all important. From years of observation I have learned that a good mechanic requires a different tool for each type of work; that a good surgeon requires a special type of instrument for various operations; and I am quite sure that a good pharmacist cannot obtain the best results in the shortest time and at the least cost without the very best modern equipment and plenty of it.

To me it is a pitiful situation to have to extemporize some sort of equipment which will be more or less crude, to produce certain results, thereby slowing up the process and necessarily increasing the cost of production, when the expenditure of a relatively small amount of money would increase production and lower costs. Therefore, from a standpoint of economy I would recommend that hospitals supply their pharmacies with all the needed machinery and other equipment. And this brings us back to the needs of the individual hospital.

Perhaps there are many smaller hospitals which do not use sufficient quantities of one type of preparation to warrant an expenditure of any great amount of money for machinery and other equipment yet when we compare the cost of making a preparation with that of buying the same preparation through the ordinary channels it proves that the price of the equipment is soon saved. I should like to cite one specific example. During one month, recently, our records showed that the difference in cost of manufacturing a few of our much-used preparations, as compared with what we formerly paid for them, saved our hospital something over $300.00, and this can easily be repeated twelve times a year and increased to almost any extent by adding new items to the list.

As a suggestion to those who have not tried out this idea, I mention a few of the more simple and easily made, as well as useful and essential preparations needed in every hospital, which can be made without any great expenditure for equipment: Sterile Lubricating Jelly, Antiseptic Baby Oil, Food Flavorings, Permanent Writing Fluid, Pathological Dyes and Stains, Milk of Magnesia, Hand Lotions, Certified Food Colors, Polishes (furniture, silver, brass, copper), Red Ink, Urinalysis Solutions. It is imperative that the preparations thus made be equal in quality to any that may be purchased.

Recently we have heard much and read more concerning the "Hospital Formulary." Many hospitals have been using a formulary for some years and no doubt many of them successfully, but I am doubtful of the advisability of adopting them in all types of hospitals. If it is in a private hospital, to which my experience has been limited, it seems ill-advised to try to tell the some two hundred physicians who practice within the institution that we limit their prescription-writing to such preparations as might be agreed upon by a certain group.

It has been our custom to take care of any and all prescriptions although we try to discourage the use of the same, or very similar formulas, which may appear under

several trade names; and whenever possible to suggest the use of U. S. P. or N. F. preparations by contacting our physicians.

In a National, State or Municipal hospital I am aware that it may be possible to limit the number of items to be used, because such institutions, as a rule, are not so dependent on the goodwill of the medical profession.

Personally I feel that a patient entering a hospital for medical treatment, is entitled to any preparation, however rare or expensive, that the physician may prescribe. The patient expects the best service that the physician and hospital can give and rarely have I heard a complaint from a patient regarding the medical charge. It is much easier to prepare a lot of stock prescriptions to be handed out by number, but, to my way of thinking, extemporaneous prescriptions are far more interesting. They require more professional ability, give the physician a greater latitude in the choice of medication, and probably increase the revenue of the hospital.

In my opinion the lot of a hospital pharmacist is one of great responsibility. He must be conscientious, accurate, alert and faithful, never failing to remember that many lives are in his hands.

IF THEY ONLY WOULD!*

BY CLARENCE M. BROWN.[1]

If all proprietors or managers of drug stores would only give as much time and care to the selection of employees as they do to the selection of a new line of merchandise or to store fixtures, time and money would be saved and the volume of business increased. A poor employee is a liability. The old method of figuring profit on cost has been discarded long ago. It is time now to discard the trial method of hiring employees; to know the possibilities of a man before hiring him. In buying a yard of cloth, one expects to receive a full thirty-six inches; therefore why not measure the man we expect to employ? There are methods for measuring capacity and ability; some are psychological, others are physical in nature.

Physical measurements are older than the psychological. They were fundamental to the homes of our forefathers. The eldest son was either taught the trade of his father, or was apprenticed to another tradesman for training. During the training period he received little or no payment other than his "keep." After a certain trial period he was accepted as an employee or rejected as being unfit for that particular trade. To-day the applicant for a position is given a brief trial period at some particular type of work, lasting from a few days to a week or month. Whether or not the applicant is aware that he is on trial, he often finds himself apparently dismissed without warning, because he has been found lacking in ability to fill the position in a satisfactory manner and two people have suffered loss—the prospective employer and employee. For janitorial work the trial test period (physical test) is perhaps the only satisfactory means for determining fitness of the applicant.

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* Presented before the Section on Pharmaceutical Economics, A. PH. A., Minneapolis meeting, 1938.

[1] Professor and Secretary of the College of Pharmacy, Ohio State University.

For clerical and sales positions, physical tests are impractical to say the least. In the past, such tests, either with or without "recommendations," have been practically the only available means of judging ability. Yet to find a person incompetent after a lapse of even a month is a waste of both time and money; psychology, therefore, has been called to the aid of industry in providing means for measuring with a degree of accuracy the capacity for selling.

No individual can do all things equally well, however nearly he may seem to do so. There is always some one thing that is done better or more easily than anything else. There is an innate capacity to do that thing exceedingly well. Capacity is not ability. Psychologically these terms differ. Capacity limits ability. Training will increase ability but not capacity—hence ability may vary from day to day or from hour to hour, but capacity has a maximum development beyond which it cannot go. Therefore, one's capacity to do a certain type of work is limited, but one's ability to do more work of a definite type or to do it in a better way may be increased by training or by previous experience.

Some individuals will never be good salesmen, but will be excellent registered pharmacists or laboratory technicians. Others may be both salesmen and registered pharmacists, but are not equally good in both positions, although to casual observation they may seem to be so.

Pharmacists, as a rule, employ help by the usual method of depending upon letters of application, letters of recommendation, upon personal interviews or after they have "read character" from appearance of the applicant's handwriting or what not. So firm a hold has character reading upon certain individuals that no amount of argument could possibly weaken their faith in their own ability at judging people from appearance. If each of the three components upon which judgment is based is held up to the cold light of reason, each will be found to be wanting in dependability.

I. The letter of application, if lengthy, is really more or less a flattering autobiography—all the good points and none of the bad. If the letter is brief, then it serves merely as a means of introduction between applicant and prospective employer. Much has been said in school and out regarding character as revealed by the letter of application and that it therefore should be in one's own handwriting. It was considered a definite proof of carelessness if not all i's were dotted, not all t's crossed and all letters not of a corresponding height and slant. Many tests[1] given college students have proved that there is no scientific basis for assuming that an individual's handwriting discloses his capacity for work. Neither is there any real basis for judging character in this manner. If character were so disclosed, many of us would be beyond the pale of respectability. Dr. A. T. Poffenberger[2] claims the validity of estimation of character from letters of application is only about twenty per cent better than can be estimated by chance. However, the fact that a neat letter of application produces a pleasant first impression upon the reader must not be overlooked. First impressions are, however, often wrong in regard to true traits of character and ability.

II. The letter of recommendation is also a help in judging an applicant, but not to the extent that some pharmacists believe. Such letters are usually written

[1] By Dr. Clark L. Hull, University of Wisconsin.

[2] Psychology of Selecting Employees, Laird.

by friends. Naturally only the best qualities of the applicant are mentioned. Unless the prospective employer is acquainted with the writers, such letters are apt to be rather inaccurate as to facts. If written by former employers, and especially if the writers are known, more dependence can be placed in them since a truer picture of the capacity and ability of the individual is usually given as a matter of confidence.

III. In granting a personal interview it should be remembered that in judging an individual for the six most necessary characteristics for success; namely, common sense, energy, initiative, leadership, reliability and general ability,[2] judges agree among themselves to only 21% more accuracy than would be indicated by mere chance. The personal interview, then, depends to a great extent upon the interviewer or judge. A single characteristic may cause a favorable reaction upon one employer but an unfavorable one upon another. Do not feel too certain of the infallibility of your own ability to "size up" an individual. An interesting experiment was conducted by Prof. D. A. Laird[1] in which "Twelve sales managers with considerable experience in selecting representatives by personal interviews took part. Each manager interviewed the same fifty-seven candidates and ranked them from one to fifty-seven. The candidate that was ranked one by one manager was ranked fifty-third by another and fifty-seventh by still another. In no case was there any agreement as to the ranking of any single candidate."

Another interesting experiment is reported by Dr. Walter D. Scott[1] in which a number of employed salesmen were interviewed without knowledge of their productive record. Later the rankings of these men as given by the interviewers were compared with that as shown by their productive records. Only one of the interviewers succeeded in placing the best salesman in the same position of rank as given by his productive record.

These experiments would tend to show that the interview while helpful in judging personal appearance, speech and general impression of an applicant, does not give an accurate estimation of capacity for doing the job well. These first impressions as obtained by interviews are desirable in a salesman, as his ability to make a good impression on the customer is advantageous. But first impressions are not enough. Other characteristics should be discovered to indicate capacity. To be able to decide that Jones has the capacity for making a good salesman after due training is far more important than to hire him simply because he looks like the best man. Interviews alone should not be the sole means of judgment but if well planned are of value in the speed with which many applicants can be temporarily classified.

Before employing an applicant a well-planned interview should establish something concerning the applicant's family history, his educational background and his social habits, as well as his personality and physique.

There must be no home conditions that would tend toward a mental fog or confusion between attention to work and marital troubles. Heavy indebtedness or a large number of dependents are trouble makers. To have parents who have had the advantages of an education or if lacking an education themselves have been in sympathy with his educational efforts, is a decided help to an individual in the development of a correct attitude toward employment and employer. An appli-

[1] Psychology of Selecting Employees, Laird, McGraw-Hill Book Co., Inc., 1936.

cant whose father has been employed for a long period of time by one firm is very apt to dread unemployment himself and also to understand that every position has its disadvantages.

The social habits have made or broken many men. To live socially within one's means is indicative of honesty. There should be no indication of strong anti-social or political tendencies that might lead to difficulty with customers or other employees. To be well informed upon current events points toward leisure time well spent in reading and in social contacts.

To have established some or all of the above facts concerning an applicant has given value to the personal interview, but has not established the capacity of the individual for the position. The facts obtained by the interview should be noted for comparison with those obtained from interviews with other applicants. It is well to have a typed interview form to be checked, unobserved if possible, during the interview. Facts are easily forgotten or confused after several interviews.

A second interview should be arranged with each applicant within a very short period of time. Each should be told frankly that others have applied and that a little time will be needed to decide matters, and that in the meantime he too can decide whether or not he will be satisfied with the salary and conditions specified. If the plan is to use some of the modern psychological tests to determine "capacity," then before dismissing the applicant he should be taken on a brief inspection trip through the store. Locations of various classes of merchandise should be pointed out. He should be introduced to those who may be future co-workers. The purpose of all this is to see the reactions of the applicant and of the other employees. Does he seem to understand what is being told him? Was he friendly toward those he met? What were the reactions toward him?

At the second interview the selective process can be carried still further. At this time it can be explained to the applicant by way of introduction to a written test that will follow that the ability to think quickly and logically and to work rapidly and carefully are necessary qualifications for a good drug clerk. These statements should be made in such a manner as not to cause excitement.

These written tests are psychological in character and are so devised as to measure the capacity of an individual for certain types of work. They are standardized and copyrighted and must therefore be purchased from the proper sources. For this reason only the objective of each set of papers is given here. These copyrighted tests are of two types:

(A) General Capacities
- 1—Intelligence
- 2—Good judgment in various social positions
- 3—Recognition of mental states from facial expressions
- 4—Memory for names and faces
- 5—Close observation
- 6—Social information
- 7—Fundamental mathematics involved in the making of change and in the selling of merchandise.

(B) Specialized
- 1—General clerical; spelling, grammar, filing, etc.
- 2—Various others which are industrial in character.

To many pharmacists this method of employing will seem to be unnecessary and even foolish. If this be true, why then do the employment offices of many of the larger department stores and manufacturing concerns use it? Is it not true that the usual "trial" method of hiring drug store help has too often resulted in loss of time and money?

For the very small neighborhood store such a lengthy procedure of selection may be unnecessary. In such a store, closer personal observation by the proprietor is possible. Too frequent changing of clerks is bad for any store or business. Drug clerks usually quit their job for the following reasons:

(A) Better offers elsewhere

1—Better hours
2—Larger salary
3—Better working conditions

(B) Misfits

1—Accepted position because they could not get anything else at the time
2—Mistaken in thinking they would like the drug business
3—Lazy—"too much work"
4—Are not lazy but have no capacity for salesmanship.

Employers should realize that no one man can be expected to do the work of two and be content in doing it. No one likes to be forced to work twelve to fourteen hours on Sunday, without time for lunch or dinner. No one likes to be relieved at six-thirty or seven, when he is supposed to leave at six. No one likes to replenish stock and trim windows on Sunday, even though one is on duty. On this day one should not be required to do more than wait on patrons or make out necessary reports or orders. This is also true of evening work. Every clerk should be given some time for reading of trade journals when not actually busy in waiting upon customers.

On the other hand, employees should realize and be told that they too are expected to be prompt when reporting for work; that they are expected to keep the store clean and neat; that they are expected to keep the stock in condition and not neglect to order items when low. Every employer has a right to expect his help to keep themselves physically fit. Every salesman should seek information from every possible source concerning the merchandise he is selling. Moreover he should be well informed upon the latest medical advancements.

In summary it can be said that no one can be happy trying to do something which is unnecessary and therefore distasteful; no one can be happy doing work for which he has no capacity; and no amount of training will overcome lack of capacity. Therefore, since capacity is a very fundamental requirement for any position, why not test for it? If they only would!

LIST COAL-TAR COLORS SUITABLE FOR USE IN FOODS, DRUGS AND COSMETICS.

The Secretary of Agriculture has promulgated regulations under the new Federal Food, Drug and Cosmetic Act listing more than a hundred coal-tar colors and providing for certification of batches of these colors as harmless and suitable for use in foods, drugs and cosmetics. The regulations are based upon evidence which was submitted at public hearings in February, became effective immediately upon their publication in the Federal Register on May 9th, and can be obtained from the Superintendent of Documents, Government Printing Office, Washington, D. C. The price of a single copy is 10 cents.

COMPARISONS AND CONTRASTS OF CONDITIONS OF PHARMACY IN THE UNITED STATES AND OTHER COUNTRIES.*

BY INA GRIFFITH.[1]

For some time I have been interested in the conditions of Pharmacy in this as compared to those in other countries, and for the past year or more I have carried on an active correspondence with women pharmacists in several foreign countries. The results of this investigation are recorded in two parts; *first*, those aspects of Pharmacy which particularly affect women; and *second*, the conditions of Pharmacy in general, affecting both men and women.

In pursuing this subject I carried on a correspondence with twenty-five or more women in the West Indies, Europe, Asia and Africa. The results and conclusions are drawn from some sixty replies. It may be interesting to know how my correspondents were chosen. I consulted the "Index Generalis" in the University of Oklahoma Library for the names of the deans or directors in every country maintaining a school of pharmacy and asked them to send me the names of outstanding women in the profession in their various countries. The response has been most gratifying.

Time does not permit telling all the interesting incidents of my correspondence but in general it was grouped around the following list of questions:

What is the percentage of women pharmacists in your country?
What type work are they doing in the profession?
Are there organizations for women in Pharmacy in your country?
Does the wage scale discriminate between men and women pharmacists?
Do the duties of your pharmacists extend beyond that of selling drugs and filling prescriptions, such as diagnosing and prescribing?
Are your drug stores open for business on Sunday?
Are your drug stores open at night?
What are the entrance requirements in your school of Pharmacy?
What type of work is taught in your school of Pharmacy?
How many years work are required for completion?
Are your pharmacists required to have practical experience before they complete their course for graduation?
Are pharmacists in your country granted a license to practice?
Are your pharmacists required to have practical experience before becoming licensed?
Are your pharmacists required to take an examination before they are permitted to practice?
Must your drug store owners pay a license fee to operate?
Are there regulations in your country concerning the number of pharmacies that may be established?
Is there a close relationship in your country between the pharmacist and physician?

There is no doubt that the facts are authentic because in each case my correspondent was either a member of the faculty of a school of pharmacy, a hospital pharmacist, an analytical pharmacist or a drug store owner.

Letters have come to me from seventeen countries and it is interesting to note that in only three countries is the percentage of women pharmacists as low or lower than that in the United States. The correspondent in India stated that there are

* Presented before the Section on Education and Legislation, A. PH. A., Minneapolis meeting, 1938.

[1] Instructor in Pharmacy, University of Oklahoma, Norman.

no women pharmacists there. In Egypt the director of the school told me that women entered their college of pharmacy last year for the first time; three are now enrolled. In the Lebanese Republic women were not permitted to enter Pharmacy, Medicine or Dentistry prior to 1920, and I'm not sure of the percentage at present.

In Argentina, Cuba, Estonia, France, Poland, Lithuania and Roumania, from fifty to sixty per cent of the graduates are women, while in Denmark, England, Greece, Hungary, Italy, Norway and Switzerland the range is from ten to thirty-five per cent.

In most of these countries there are no pharmaceutical organizations for women but the women enjoy equal rights with the men in any pharmacy organizations in existence. There is a women's organization in France but it is not of much importance, while in Poland there is a department for women in the National organization. In England the National Association of Women Pharmacists was formed about the beginning of this century by a small group who felt the need for close coöperation among the women who were entering a new profession. All women pharmacists are eligible for membership. The objects of the organization are three-fold and are stated as follows: (1) The consideration and discussion of all matters affecting women pharmacists; (2) To keep a register of those members desiring employment and to bring employees into touch with employers; (3) The promotion of professional and social intercourse among the members.

The organization maintains both an employment bureau and a loan fund. The loan fund was founded to give assistance to members in cases of distress, illness or other emergency. There are now over 3,000 women on this association's register and one correspondent states she has watched conditions for women improve steadily during the past twenty years due to the activities of this association.

In answer to my question, "does the wage scale discriminate between men and women pharmacists," from France, Hungary, Poland, Norway, England, Italy and Estonia replies came that there is no discrimination. However, in Hungary the men have the advantage of obtaining state employment and in Poland, since the number of women pharmacists exceeds the men, the latter are more in demand, hence often receive higher salaries. In Italy and Estonia the wages are governed by a fixed scale. Regardless of the wage scale the information comes that the women are performing their duties nobly and that as a whole they greatly please their clientele. Women pharmacists in these seventeen countries do much the same types of work in the profession as they do in this country, that is, they are pharmacists in stores, owners of stores, hospital pharmacists, analysts in laboratories and teachers.

I was interested in the type of training these foreign co-workers received, also any other requirements they must meet. In Switzerland those who aspire to become pharmacists spend six and one-half years in preparation. After the first two years in the university the student spends eighteen months as an apprentice without pay. At the close of this period he passes an examination and receives the first diploma which entitles him to fill an assistant's post. He must remain thus one year before going on with university work. After two more years in the university the final diploma is granted which entitles the pharmacist to own his

store or to be a manager in any Swiss pharmacy. A license to practice cannot be refused a graduate who passes his final examination.

In Norway only thirty students per year are permitted to enter the study of Pharmacy and these by permission of the professors of the institution. The thirty are selected from those passing an examination. To become a store owner one must have the education, the required years as a pharmacist in a store, the money, a vacant store, and last but not least, the recommendation of the Department, then the King will allow the applicant to obtain a store.

The number of students in Hungary entering Pharmacy is limited and it is extremely difficult to be admitted. The children of pharmacists or "chemistry" owners, as they are called in Hungary, are given preference. Their training consists of two years practical work at a dispensing chemistry, followed by a two-year course at the university. When this training is completed the individual may be employed in a chemist's shop. In order to own a shop or be a responsible head of one, two additional years training are necessary. This work is usually combined with a paid position in a chemist's shop. At the completion of the university work the pharmacist must pass an examination which qualifies him to practice.

In Greece the individual planning to enter the pharmaceutical profession must work in a pharmacy one year, then undergo an examination before he is allowed to enter the school. The school work lasts for four years with annual examinations and a final examination, written, oral and practical. However, before the students are permitted to practice they must yet work a year in a pharmacy and finally pass an examination given by a special Government Commission called the Highest Sanitary Commission.

In Poland, Italy and France those who aspire to become pharmacists must have one year practical experience and four years study at the respective universities. Training in Poland includes examination of food articles and bacteriology so the pharmacist may serve as an expert witness in legal proceedings. I was interested to note that this training to be an expert witness seems of great importance. Before being permitted to practice, the Italian pharmacist must pass an examination termed the "State's Examination." In both Italy and France the store-owner must pay a license fee in order to operate.

The prerequisite for the practice of Pharmacy in Estonia is four years' study at the university and two years' practical experience followed by an examination. Upon passing this examination the individual becomes a full-fledged pharmacist. Each year the druggists of Estonia must obtain a new license which permits them to operate.

My Estonian correspondent has been most gracious in answering my questions. The mass of statistics she had available seemed amazing. One striking point of interest was, in December 1936 one hundred ninety-five women and eighty men were studying Pharmacy while in September 1937 there were only twenty-four women and six men. This decrease can be explained because a ruling was made that only thirty students were allowed to enroll.

Since in many of our towns and cities we have an excessive number of stores for the population I was interested in the conditions elsewhere. I discovered that in most of the countries interviewed the number of stores per population is

restricted. In those countries where restrictions are not in effect the correspondents felt they were desirable. In Denmark the establishment of a pharmacy is a privilege distributed by the state. In smaller towns there are one, two or three stores while in Copenhagen, a city of 800,000 inhabitants, there are sixty-five stores. In Estonia the number of stores per city is also limited. There are 1,200,000 inhabitants and only two hundred ten drug stores, one hundred ninety-two of these stores are privately owned and eighteen belong to either the national or city governments. Only a limited number of pharmacies may be established in Hungary and those upon license from the Ministry of the Interior. In Italy and Roumania the number is limited to a pharmacy for each 5,000 inhabitants. The concession system also exists in Poland, but the government reforms tend to abolish the system and according to the correspondent the future of the apothecary shops is not very bright. Switzerland has no regulation as to the number of pharmacies that may be established but my correspondent informed me that too many pharmacies had been opened and that they are trying to get such a regulation. The number of stores in France is very high and there is no restriction, but according to the correspondent restriction is desirable.

The problem of late hours and Sunday practice is keenly felt in this country. I was interested in the attitude of these other countries toward this subject. From England the information comes that the hours are long, but they vary in different districts. The city shops may close at 7:00 P.M., but in the suburbs they remain open until 9:00 P.M. on Saturdays. The shops are usually open on Sunday, but many districts have a schedule whereby every shop is open only one Sunday in three or four weeks.

In Denmark the system is a little more attractive. On Sundays the drug stores are open in towns or cities where only one is located and in those with more than one store they stay open in turn according to a voluntary agreement. The arrangement for night service, that is from 6:00 P.M. until morning, is in accordance with Sundays as to turn, but only a single pharmacist is present, and must be called by a special bell. It is interesting to note that a small extra fee of about twenty-five cents is charged.

The French apothecary shops also have an arrangement where one or more, depending upon the importance, are open on Sundays and Holidays. In the window of a closed shop is a card indicating the address of one in the neighborhood which is open so those in need of medicine never have to be without.

The pharmacies of Greece are open ten hours a day. The opening and closing time being changed according to the season.

In Hungary only those stores designated as "on duty" are open at night and on Sunday until evening, while those not "on duty" are open on Sunday from eight until 1:00 P.M.

From Italy the information comes that one-third the total number of stores in a town are open on Sunday and their time comes by turn. There is no special rule for the night work over all of Italy but in Pisa a hospital store is open until midnight and also a store on one of the main streets, but to remain open all night a special permit is necessary.

In Polish towns in which there are more than one store, by agreement they are kept open at night and during Holidays by turns. In the other towns, as the cor-

respondent expressed it, they are open constantly, Sundays, Holidays and nights.

In most towns in Switzerland there is an arrangement between pharmacists for Sunday and night duty. The hours vary with the towns. In Vevey, the home of the correspondent, the plan for a year is settled in advance. The store which has Sunday duty starts on Saturday night and has night duty as well, all week. The store remains open until 10:00 P.M. and, after this, the pharmacist answers a night bell. A fee of two francs is asked from every customer after 10:00 P.M. and until 8:00 A.M., when the store is reopened.

In Lausanne, Switzerland, the pharmacies close in turns at 7:00, 9:00 and 11:30 P.M. and none are open after that hour. A few medicines are deposited with the police and the doctor who needs them goes there and helps himself.

Since the majority of drug stores in this country carry a variety of merchandise, and the pharmacists are accused of counter prescribing, I wondered if these conditions existed elsewhere.

The English correspondent informs me that a certain amount of counter prescribing is done but that for the most part diagnosing is left to the doctor.

In Denmark pharmacists are prohibited to either attempt diagnosis or prescribe, these duties being reserved for the graduated physicians. Of Estonia we learn that the stores selling cosmetics, paints and patent medicines have nothing to do with Pharmacy. According to the correspondent the drug stores of Estonia cannot be compared with the American drug store because they are strictly medicinal institutions. They are subordinate to the State Sanitary Commission and to the Health Commissioner, consequently one speaks not of drug business but of drug service.

My correspondent in France informs me that the present laws regulating pharmacists' requirements are based upon an old law which goes back to 1803. The substance of that law as she gives it is, "Pharmacists will not be able to make or sell medicinal preparations or any mixed drugs whatsoever except after a prescription which will be made by Doctors in Medicine or Surgery or by Health Officers, and on their signatures. They will not be able to sell any secret remedy, they will comply with the formulas of compounds which they must execute and hold in their pharmacy; these formulas are inserted and described in the Dispensatory or Formulary which has been drawn up, or are to be so in the future, by Schools of Medicine. They will not be able to make in the same offices any other sales except that of drugs or medicinal preparations."

In Hungary pharmacists sell drugs only, compound prescriptions and do some chemical investigation. Only doctors diagnose and prescribe. In Italy the same conditions exist as in Hungary.

My correspondent of the Lebanese Republic tells me she is the only woman who owns a drug store; incidentally she is a graduate of the University of Maine, and Harvard. She has two stores, one in Beyrout, which she closes during the summer and another at a summer resort which she operates during the summer. At her store in Beyrout she sells only medicines and toilet articles, while in the store at the summer resort, "like the American drug store, I carry everything even Ice Cream." She tells me she had a hard time getting the confidence of the people. She has become noted for making all kinds of toilet creams.

The Polish pharmacist can only prepare and dispense medicines according to the written prescription of the physician, who alone has the right to visit the sick, diagnose the case and prescribe the medicine. A few milder medicines can be sold by the druggist without a prescription.

The pharmacists of Switzerland sell only drugs and compound prescriptions. They do not diagnose or prescribe except in minor ailments. Physicians are not allowed to dispense their drugs unless they are a certain distance from a pharmacist, except in one or two districts which have their own laws on the subject.

From the foregoing comparisons and contrasts it seems to me the following conclusions can be drawn:

1. Women have a definite place in the pharmaceutical profession abroad.
2. The number of women in Pharmacy in some foreign countries averages considerably higher than in the United States.
3. Training for pharmacists abroad is more rigid in many instances than here, and longer apprenticeship is required.
4. It appears that incomes from Pharmacy in these countries are more stable, possibly due in part to the concession system.
5. Experience in some of these countries demonstrates that the public can be educated to make purchases at hours other than at night, or on Sunday or to pay an extra fee for this service.
6. The impression given me by my correspondents indicates that these countries look upon Pharmacy as a serious and exalted service. The emphasis upon the professional side far outweighs the mercantile aspects. One correspondent called my attention to the fact that the term "drug business" is not known but the term "drug service" is used.

AQUEOUS ELIXIR—PROPOSED CHANGE IN FORMULA.*

ADLEY B. NICHOLS AND GERALD S. SAVITZ.[1]

In presenting one of the annual exhibits of the National Formulary at the Convention of the American Medical Association, one of the writers was quite surprised to find that a freshly prepared aqueous elixir had turned from a colorless solution to one with a faint pinkish tinge, from the time it had been shipped to the time the material was opened for display, a matter of only a few days. Upon returning home a check was made upon a sample prepared some time previously, and it was discovered that this also had changed color, having a decidedly reddish cast.

Recognizing the nature of the vanillin which is contained in the preparation, it was surmised that this might be the troublesome factor. In this respect it was recalled that the delightful Compound Elixir of Vanillin of the N. F. was also subject to some darkening upon aging, probably due to the same general cause. A

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* Presented before the Section on Practical Pharmacy and Dispensing, A. PH. A., Minneapolis meeting, 1938.

[1] Pharmacy Laboratory, Philadelphia College of Pharmacy and Science, Philadelphia, Pa.

few experiments soon indicated that the item in question was none less than the vanillin, since only the elimination of the vanillin produced a stable product, the color changing in a short period of time.

A series of experiments was performed using various antioxidants together with a control, only to find that the usual change did not occur even in the control. Then it was discovered that a lot of vanillin from an entirely different source had been used and since screw-cap bottles had been employed in place of the cork stoppers previously used, a series of elixirs was prepared using the original type of vanillin, screw cap and cork stoppered bottles and various antioxidants. Within ten days to two weeks time color changes were noted in all except those in which sodium formaldehyde sulfoxylate had been used. The latter are still colorless at this writing, after a period of more than five months.

Believing that there might be a difference in the various vanillins which are available, possibly due to differences in purity or origin, whether made from clove or guaiacol, authentic samples of both varieties were obtained from manufacturers. These, together with several other available lots, were used to prepare the elixir in question. After aging for three weeks there is no perceptible change in any of the preparations, and time alone will tell whether or not material differences will develop. If differences are noted it will then be necessary to determine the true causative factor.

Vanillin of course acts like a phenolic body and would readily give color reactions with various impurities. It seems to be recognized generally that a trace of iron will cause its solution to change color; light is believed to affect it and there is the possibility of certain impurities not being removed during the manufacturing process, although it is conceded to be quite thoroughly purified on the whole.

Regardless of the final outcome as to what is causing the specific color change, and whether or not it will be of such a nature as to be corrected readily, it would seem desirable that the formula for Aqueous Elixir be changed to provide a colored vehicle rather than the water-white colorless preparation now official. As a vehicle to improve the appearance as well as the taste of medicines, a colorless product offers little. How much more pleasing and attractive to the average individual does a bright-colored prescription appear! It looks appetizing to begin with, and that in itself is a most valuable asset.

Therefore it is suggested that to the present Aqueous Elixir formula be added 5 cc. of the official solution of amaranth for each 1000 cc. of elixir. The elixir then becomes bright red in color, beautifully clear and sparkling if well prepared, considerably more attractive as a general vehicle for prescription usage, and the natural red color would be sufficient to successfully mask the possible color change previously mentioned.

The Fourth Annual Bronx Better Health Week convened at Fordham University, College of Pharmacy, New York City, on May 3rd and 4th. The program was devoted exclusively to the control of Diabetes and its complications.

The Medical Association of Alabama held its annual session in Montgomery on April 18th to 20th. Dr. A. R. Bliss, Jr., presented a paper on, "A Plea for the Use of Pharmacopœia and National Formulary Drugs."

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1938–1939.

Office of the Secretary, 2215 Constitution Ave., Washington, D. C.

LETTER NO. 7.

April 6, 1939.

To the Members of the Council:

56. Use of Text of N. F. VI. Motion No. 16 (Council Letter No. 6, page 249) has been carried with the following members voting in the affirmative: Co, Ro, Ch, Fi, Du, Mo, Li, Sw, Hi, La, Ke, Je, Ga, Dm, Ck.

57. Research Grant. A vote is now called for on Motion No. 17 (Council Letter No. 6, page 250) and voting card is attached. No comments have been received to date.

58. Election of Members. Motion No. 18 (Council Letter No. 6, page 249) has been carried with the following members voting: YES, Co, Ro, Ch, Fi, Du, Mo, Li, Sw, Hi, La, Ke, Je, Ga, Dm, Ck.

59. Rhode Island College of Pharmacy and Allied Sciences Student Branch. Motion No. 19 (Council Letter No. 6, page 251) (Please correct your records) has been carried with the following members voting in the affirmative: YES, Co, Ro, Ch, Fi, Du, Mo, Li, Sw, Hi, La, Ke, Je, Ga, Dm, Ck.

60. The Connecticut College of Pharmacy Student Branch. The following application accompanied by the membership applications and the dues for the signers together with the proposed Constitution, has been received:

"We, the undersigned students of The Connecticut College of Pharmacy desire to establish a Student Branch at our school and petition the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION to approve the formation of the Branch.

Abraham Wolfthal	John P. Hoyt	Lillian Lavieri
Jacob J. Krivitsky	Jacob A. Kraut	Benjamin J. Frankel
John Polonsky	Rosario Calvo	Robert S. Althen
Andrew Kusaila	Edward Honiberg	Charles Blumenthal
Everett B. Mott	M. M. Zimmerman	Harold N. Dinerstein
Jack N. Etelis	Freda Mekrut	Morton I. Benzel
Lewis Reese		Robert L. Doane

The following officers for the Branch were elected: *President*, Abraham Wolfthal;, *Vice-President*, Milton Zimmerman; *Treasurer*, Jacob Kraut; *Secretary*, Charles Blumenthal; and Dean Henry S. Johnson has been selected as *Faculty Advisor to the Branch.*

PREAMBLE.

We, students of the Connecticut College of Pharmacy, with a pride in and a devotion to the ideals of the profession we have chosen to follow, do hereby constitute ourselves into this organized body as representative of the AMERICAN PHARMACEUTICAL ASSOCIATION, pledged to foster and further its program. We seek to preserve and protect Pharmacy as a profession, ever progressive and elevating its standards, and do hereby adopt this constitution and by-laws.

CONSTITUTION.

ARTICLE I.—*Name.* This organization shall be known as, "The Connecticut College of Pharmacy, Student Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION."

ARTICLE II—*Purpose.* It shall be the purpose of this organization to uphold the aims, and to aid in the pursuance of the program set forth by the AMERICAN PHARMACEUTICAL ASSOCIATION. Further, it shall undertake a feasible scheme of activity, calculated to promote scien-

tific investigation, professional interest and an esprit de corps among students of Pharmacy with whom it may have contact.

ARTICLE III—*Membership.* Section 1. The members of this branch shall be elected from among the bona fide students of the Connecticut College of Pharmacy, who have met the requirements for associate membership in the AMERICAN PHARMACEUTICAL ASSOCIATION.

Section 2. Two members may submit the name of a candidate to the chairman of the membership committee, who will present the name of said candidate at the next meeting of the branch. In the absence of the candidate a vote shall be taken by secret ballot. A three-fourths vote of those present shall elect a candidate to membership in the branch.

ARTICLE IV—*Officers.* Section 1. The officers of the Branch shall be: (*a*) A president, (*b*) a vice-president, (*c*) a secretary, (*d*) a treasurer.

Section 2. Election of officers shall take place annually at the last meeting of the academic year. A majority vote taken by secret ballot shall be necessary to elect an officer, after nominations from the floor. These officers shall be installed at the first meeting of the next academic year.

Section 3. The duties of the officers shall be described in the by-laws of the branch.

ARTICLE V—*Committees.* Section 1. The following committees shall be permanent standing committees of the branch; they are to be appointed by the president at the first meeting in the academic year. (*a*) A program committee, to consist of four members and the vice-president. (*b*) A membership committee, to consist of three members. (*c*) A public relations committee, to consist of three members, one of whom shall be the secretary. (*d*) A trustees committee, to consist of three members.

Section 2. The duties of these committees shall be described in the by-laws.

ARTICLE VI—*Meetings.* Meetings shall be held at least once a month, and at any other time that may seem advisable to the officers. Every member shall receive due notification of each meeting at least one week before it is to be held.

ARTICLE VII—*Quorum.* Nine members, including at least two officers, shall constitute a quorum, except at elections, when three-fourths of the total membership shall be necessary to hold a meeting.

ARTICLE VIII—*Fiscal Year.* The academic year shall constitute the fiscal year.

ARTICLE IX—*Presiding Officer.* In the absence of the president the next succeeding officer shall take the chair according to the following order: vice-president, treasurer and secretary.

ARTICLE X—*Amendments.* This constitution and by-laws or any part thereof may be amended or repealed by a two-thirds vote of the members.

BY-LAWS.

1. *Duties of the Officers:* (*a*) The president shall preside over all meetings of the branch appoint all committees, present all bills and expenditures before the branch, and upon a majority vote shall instruct the treasurer to make payment. (*b*) The vice-president shall exercise the duties of the president in case of his absence and shall act as the chairman of the program committee. (*c*) The secretary shall keep a record of all meetings. He shall prepare and forward reports of such meetings, and any other correspondence necessary, to the secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION. He shall keep records of all correspondence received or entered into by the branch. He shall notify each member of the branch of the time and place of all meetings. He shall also act as the chairman of the public relations committee. (*d*) The treasurer shall keep a record of all funds of the branch. Before the last meeting of the fiscal year he shall present to the trustees committee, a financial statement, for their approval. He shall make all remittances to the secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION as are necessary, upon receipt of funds for dues from the members, in the manner prescribed by the rules of the AMERICAN PHARMACEUTICAL ASSOCIATION. He shall present all bills and expenditures to the president as provided in part (*a*) of this section. He shall issue duplicated receipts for all funds received, and obtain receipts for all funds issued. He shall preserve a record of all such transactions.

2. *Records of the Meetings:* Records of the meetings of the branch shall be issued by the secretary in copies sufficient to provide one for each member of the branch.

3. All records of the branch shall be available for examination to any member of the branch at any time.

4. All meetings shall be conducted according to "Robert's Rule of Order."

5. Duties of the Standing Committees: (*a*) The program committee shall prepare all programs and furnish such materials as may be necessary. The chairman shall advise the secretary of all invitations to guests, and acknowledgments relative to activities of the program committee. (*b*) The membership committee shall submit the names of any candidates for membership as provided in Article III of the constitution. (*c*) The public relations committee shall, under the guidance of the secretary, be responsible for the publicity of the branch and its activities. (*d*) The trustees committee shall review the treasurer's report and, upon approving said report, shall present it at the last meeting of the year for the approval of the members.

6. All funds of the branch shall be held in a bank account registered in the name of the branch; the chairman of the trustees committee and the treasurer shall act as cosignatories for all withdrawals from such account.

7. The branch shall enroll all members of the faculty, who are regular members of the AMERICAN PHARMACEUTICAL ASSOCIATION, as honorary members of the branch. They shall constitute a faculty advisors board.

8. Resolutions of the AMERICAN PHARMACEUTICAL ASSOCIATION, or any of its rules or laws shall take precedence over the rules or resolutions of this branch, when the two shall be in conflict.

(*Motion No. 20*) It is moved by Little that the application to establish The Connecticut College of Pharmacy Student Branch of the ASSOCIATION and the proposed Preamble, Constitution and By-Laws be approved.

61. Applicants for Membership. The following applications, properly endorsed, accompanied with the first year's dues, and recommended by two members of the ASSOCIATION, have been received:

Nos.: 521, Fred Farber, 2131 Cloverdale Ave., Los Angeles, Calif.; 522, Jacob E. Bowser, 3873 10th St., Riverside, Calif.; 523, Harry Joseph Silver, 415 S. New Hampshire, Los Angeles, Calif.; 524, Alvan Oreggia, 1153 West 37th Dr., Los Angeles, Calif.; 525, Saul Cosloy, 6253 San Fernando Rd., Glendale, Calif.; 526, Virginia Y. Bacon, 1507 Redondo Blvd., Los Angeles, Calif.; 527, Russell Meadows, Jr., 1032 West 36th St., Los Angeles, Calif.; 528, Nathan F. Sorg, College of Pharmacy, Iowa City, Ia.; 529, Arnold Moskowitz, 611 Brighton Beach Ave., Brooklyn, N. Y.; 530, C. G. Hamilton, Box 517, Pompano, Fla.; 531, Louis A. St. Germain, 612 Pawtucket Ave., Pawtucket, R. I.; 532, Abraham Wolfthal, 421 Catherine St., Bridgeport, Conn.; 533, Robert L. Doane, N. Main St., Essex, Conn.; 534, Morton I. Benzel, 35 Harding Pl., New Haven, Conn.; 535, Harold N. Dinerstein, 59 Henry St., New Haven, Conn.; 536, Charles Blumenthal, 26 Blue Hills Ave., Hartford, Conn.; 537, Robert S. Althen, 6 Kellogg St., Windsor, Conn.; 538, Ben Frankel, 643 Iranestan Ave., Bridgeport, Conn.; 539, Lillian Lavieri, 417 East Elm St., Torrington, Conn.; 540, Freda Mekrut, 21 West Silver St., Middletown, Conn.; 541, Milton M. Zimmerman, 489 Sherman Parkway, New Haven, Conn.; 542, Edward Honiberg, 1470 Albany Ave., Hartford, Conn.; 543, Rosario Calvo, 326 S. Main St., Waterbury, Conn.; 544, Jacob A. Kraut, 30 Dover St., Bridgeport, Conn.; 545, John P. Hoyt, 56 Richmond Hill, New Canaan, Conn.; 546, Jack N. Etelis, 104 Mather St., Hartford, Conn.; 547, Everett B. Mott, 17 Manor St., Hamden, Conn.; 548, Andrew Kusaila, 1284 Baldwin St., Waterbury, Conn.; 549, John Polonsky, 31 Division St., Stamford, Conn.; 550, Lewis Reese, 686 Howard Ave., New Haven, Conn.; 551, Jack Kriwitsky, 417 Garden St., Hartford, Conn.; 552, Helen Thompson, Box 612, College Station, Pullman, Wash.; 553, W. H. Whittlesey, 3527 Connecticut Ave., Washington, D. C.; 554, Marion D. Falconer, 223 E. Alberta, Anaheim, Calif.; 555, H. Pryluck, 1907 Prospect Ave., Bronx, N. Y.; 556, E. P. Stout, 14820 Piedmont Blvd., Detroit, Mich.; 557, Harold A. Bracken, 4231 University Way, Seattle, Wash.; 558, Maurice N. Powell, 7509—3rd Ave., Brooklyn, N. Y.; 559, Abraham N. Miller, 302 Flatbush Ave., Brooklyn, N. Y.; 560, Nathaniel Levitch, 302 Flatbush Ave., Brooklyn, N. Y.; 561, William Jacoff, 839 Empire Bldg., Brooklyn, N. Y.; 562, Gemma M. Folcarelli, 2676 Decatur Ave., Bronx, N. Y.; 563, Norbert G. Lassalen, 401 S. Bentalon St., Baltimore, Md.; 564, Merle M. Jackson, 6550 Marmaduke Ave., St. Louis, Mo.; 565, Kenneth S. Travers, 2329 Medill Ave., Chicago, Ill.; 566, Victor L. Threlkeld, 1804 W. Congress St., Chicago, Ill.

(*Motion No. 21*) Vote on applications for membership in the ASSOCIATION.

E. F. KELLY, *Secretary.*

PROCEEDINGS OF THE LOCAL AND STUDENT BRANCHES

ALABAMA POLYTECHNIC INSTITUTE STUDENT BRANCH.—A special meeting was called on Monday night, April 17, 1939, at 7:15 P.M., by Vice-President Charles Barron. Roll was called and minutes of the previous meeting were read and approved.

Mr. Barron opened a discussion concerning the annual banquet of the Pharmacy Department which is to be sponsored by the Student Branch. Professor Blake mentioned the fact that a committee for the purpose of inspecting the local School of Pharmacy, and a member of which is President-Elect A. G. DuMez of the AMERICAN PHARMACEUTICAL ASSOCIATION, will be in Auburn around the first of May. Some discussion followed, after which it was decided to set the date of the banquet at a time when it would be possible to have the members of the aforesaid committee present. The exact date of the banquet was then left in the hands of a previously appointed committee as it was necessary to determine the date when the visitors would arrive.

The following were appointed to collect the banquet assessment from the members of the Pharmacy Department: Mr. Lurie, freshman class; Mr. Bozeman, sophomore class; Mr. Swift, junior class; Mr. Dow, senior class. It was decided that all collections must be in by May 1.

Mr. Lurie proposed some social function other than the banquet. The motion was made and passed that further discussion on this proposal be postponed until a later meeting.

BEN EICH, *Secretary.*

CITY OF WASHINGTON.—The February meeting was held on the 13th, at the American Institute of Pharmacy. After the reading of the minutes, Mr. Hall introduced Dr. A. J. Gannon whose subject was "The National Cancer Program, with Particular Reference to the Pharmacist." Stressing the interdependence of the medical and pharmaceutical professions, Dr. Gannon outlined three ways in which the pharmacist could aid the Cancer program: (1) By disseminating information by word of mouth; (2) by discouraging self-medication; (3) by informational posters. He stated that the death rate of this disease, which takes an average of three years to kill, is about 100,000 in the U. S. annually.

Cancer is a growth that increases by cell subdivision and spreads by contiguity or through the blood stream. Some are susceptible at all ages but the rate increases over forty. It always starts locally and is not contagious. Chronic irritation on warts, skin protuberances, moles and jagged teeth, are the usual causes of cancer, also repeated changes of hot and cold. Lumps, sores, abnormal discharges, especially with blood, and indigestion, are all symptoms of cancer and should not be disregarded. The treatment consists of destroying the growth through surgery, X-rays and radium. Arsenic is a specific for certain cancers. Early diagnosis and treatment and keeping the patients away from quacks are the most effective means of combating this scourge.

When cancers get into the deeper glands which cannot be removed by surgery, the patient may be made comfortable by reducing the odor as much as possible and through the use of narcotics (not the barbiturates), to ease his pain until the end.

The Secretary was instructed to write Mr. H. Bradbury of the Drug Exchange expressing the Branch's appreciation for his assistance in distributing the mimeographed notices to the drug stores in the District.

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The March meeting was held on the 20th with thirty-four present.

After calling attention to the display of pictures of the prize-winning Pharmacy Week window displays, President Hall introduced Dr. Harry F. Dowling who spoke on "Pneumonia," which, said Mr. Dowling, "is the third greatest killer, playing second fiddle only to heart disease and cancer." It is a dramatic disease, progressing rapidly to death or slow recovery, usually attacking people in the prime of life from twenty to fifty years of age.

The pneumocci, which cause 97% to 98% of the cases of pneumonia, are divided into four types and these into thirty classes. Antisera for all thirty classes are now produced from horses although sera produced from rabbits is claimed to be more effective. Type 1 causes the largest number of cases, 31%, and reacts well to seratherapy. Type 2 is the most severe and causes 8% of the cases but does not react well to seratherapy; type three also causes 8% but does not react

to seratherapy at all. Typing is an expensive procedure and may require from ten minutes to twelve hours depending on the class. Precious time is often lost before the disease is diagnosed and typed. The serum costs $12.00 for 20,000 units and as the treatment calls for 100,000 units, the cost is $60.00.

Up till three or four years ago, no chemical agent specific for the pneumonia was known. 606 and sulfanilamide were tried. Then Main and Baker brought out 693, diagolin or sulfapyridine. It is given by mouth in tablet form, sixty tablets costing $7.20, and in such amount as to raise and maintain the concentration in the blood at a given level. The sodium salt is now produced for injection purposes. The amount required in the follow-up doses depends on the absorbability of the patient, the detoxification of his blood and the amount lost through the kidneys. Unfortunately, the drug causes certain complications such as excessive vomiting, sinosis, lymphatic anemia, and so requires that it be administered under the supervision of a competent physician. It appears to be effective against all types of the pneumocci.

A general discussion followed and Dr. Dowling was given a vote of thanks.

KENNETH L. KELLY, *Secretary.*

GREATER ST. LOUIS.—The Branch and the Alumni Association of the St. Louis College of Pharmacy held a joint meeting April 7, 1939, with one hundred present.

The subject of the evening was a description of polarized light and illustrated by a Three Dimensional Movie, in color. This movie was given through the courtesy of the Polarized Corporation and included a description of the directional control of light vibrations. The speaker stated that this directional control is made possible by a process which involves the dissolving of certain chemicals in a transparent solid material and then aligning the molecules of these chemicals in such a manner as to permit only one set of light vibrations to pass through at a time. The speaker remarked that light can be efficiently polarized with this material as with Nicol prisms.

FRANK L. MERCER, *Secretary.*

LOYOLA UNIVERSITY STUDENT BRANCH.—The regular meeting was held on March 16th, in Bobet Hall, with Joseph Ernest, vice-president, presiding.

A letter from Dr. Ernest Little, encouraging the members to keep up the good work begun, was read. A card of thanks for flowers sent Miss Heiman was received and acknowledged.

Miss Strain, acting chairman of the Membership Committee, fully described the special membership pamphlet which her committee plans to complete. Those who volunteered to do this work were: Miss Valerie Armbruster, to submit drawings for emblem; John T. Benedict, to write a brief history of the Branch; Herbert Mang, to take care of the prices and printing of such.

Miss Ware, chairman of Radio Committee, asked for volunteers who were willing to assist in writing and presenting a skit over the air. Thompson, Butcher, Bertin, R. M. Poche', Liuzza and Palmisano responded.

Miss Pitre, chairman of Entertainments, called attention to the social at the home of Miss Palmisano on April 13th, to the picnic to be held during April and the Annual Banquet and Dance, May 4th.

Mr. Thompson stated, "Last year it was decided that the pin be adopted for four years. Prices range: solid gold, $4.00; regular, $3.00; a cheaper pin, $2.00."

The "special program" was opened by Chairman Ernst in stating that this is field day for the Freshmen. Mr. Mang introduced the first speaker, John T. Benedict, who in upholding the affirmative of "Should Certificates of 'Qualified Assistants' Be Given by the Pharmacy Boards After 1937?" argued that if a man is conscientious in a certain type of work, and particularly drug-store work, he should be given every opportunity possible if he considers it to be his chosen profession for life. For this reason he favored giving Qualified Assistants' Certificates, through some type of special examination. His opponent, Ronald Macke, asserted that "if such a practice be continued the profession of Pharmacy would find itself slowly but surely losing the 'high level' it has so earnestly striven to attain." He pointed out that proprietors would aim, in most cases, to employ the men with Q. A. Certificates, because of the economy it would afford them, thus also retarding future progress of Pharmacy.

In the second debate of the evening Miss Anna Mae Luizza argued affirmatively on, "Should Drug Stores Remain Open at Night and on Sundays?" stating that Pharmacy as well as

Medicine is a servant to the public at all times, for this reason pharmacies should keep open during hours which would accommodate the many needs of the public. She further argued that as long as Pharmacy allowed itself to be a commercial institution as well as professional, the demands to serve the public will force it to keep open the hours it now maintains. Her opponent, Miss Anna Palmisano, argued that no man could expect to maintain even a minimum of efficiency if forced to work hours which will in due course of time impair his physical and mental health.

Following each of these debates there was an open forum and heated discussions arose between members and guests present.

The guest speaker was Mr. Chester A. Iorns, General Manager of Meyer Brothers Drug Co., who spoke on, "Stabilization of Prices." The theme of Mr. Iorns' speech was the abolishment of monopolies and particularly those monopolies in the drug industry which maintained unfavorable and unfair practices. He stated that, "This is not the spirit of our country and as a result, we found the tactics they employed were so destructive that in order to enforce corrective measures it was absolutely necessary to curb the activities of all on account of the actions of a few." There was a brief discussion on this topic.

Mr. Babin, president of the Branch, then introduced members of the newly formed Reception Committee: *Chairman*, Paul Poche, Miss Valeria Armbruster, Miss Elsie Strain, Gaston de le Bretonne, Clyde Simmons and Urban Hecker.

Dean McCloskey discussed, "Recent Legislation on Pharmacy Concerning Pure Food and Drug Laws."

Chairman Ernst thanked all who took part in this meeting.

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Tuseday evening, April 4th, Bobet Hall, President Babin presiding. Twenty-nine members and forty-five guests were present.

Miss Armbruster, at the request of Miss Strain, chairman of Membership, submitted preliminary designs drawn by herself and Messrs. Ernest and Benedict for a special membership folder and Mr. Benedict submitted a preliminary draft of the history of the Branch.

Miss Pitre, chairman of Entertainment, explained the arrangements for the First Annual Banquet and Dance at Arnauds' Restaurant on Thursday, May 4th; and Centanni, Ware Cassou, R. M. Poche, Thompson, Ernst, Babin, Mang and Hecker volunteered to assist the committee in making this an outstanding event.

President Babin explained how the Loyola Student Council and the Branch propose to acknowledge the work of outstanding students. A recommendation from the Council that "No organization give keys to its members unless such members have done outstanding work for the organization" was unanimously approved. A tentative note was taken on selecting one Senior, three Juniors, one Sophomore and three Freshmen considered to be the most active members of the Branch.

Mr. Vinci announced that a well-planned program including several pharmaceutical demonstrations by members of each class, has been arranged for High School Day on May 5th, and the program was approved.

In introducing the main feature of the meeting, a "Symposium on Hospital Pharmacy," President Babin stated that a principal objective was to have prominent pharmacists meet with the members of the Branch and invited the visitors to take part in the discussion. Mr. Stewart H. Butler, chief pharmacist, U. S. Marine Hospital, read a paper on, "Hospital Pharmacy and the Duties of Hospital Pharmacists," in which emphasis was placed on the rigid regulations covering the storage, preparation and dispensing of drugs and medicines. Only official articles are used in prescriptions.

Mr. A. P. Lauve, chief pharmacist, Charity Hospital, read a paper on, "Hospital Pharmacy Progress," which was followed by a paper by Miss Peggy Lou Butcher, a member of the Freshman Class, on, "What We Have Gained from Pharmacy."

A general discussion of these papers followed. In closing the meeting President Babin thanked those who took part in the interesting program and invited the visitors to attend the annual banquet and dance.

ROSALIE CENTANNI, *Secretary*.

MICHIGAN.—The March meeting was held at Wayne County Medical Society Building

on the 21st, preceded by the usual excellent dinner. When the meeting was called to order more than one hundred and twenty-five were in attendance.

The first of the double feature program was the showing of a moving picture film in natural color, taken by the secretary while touring Mexico. Included were many beautiful churches, the Floating Gardens, summer home of Maximilian, bull fight and many other colorful scenes in old Mexico.

The second feature was provided by Mr. Walter M. Chase of Parke, Davis & Co., who conducted a "Pharmaceutical Quiz" which not only proved most interesting but popular to the extent that the students of the Colleges of Pharmacy have asked for a return engagement of Prof. Walter "Quiz" Chase.

The contestants represented all phases of Pharmacy. H. A. K. Whitney, Hospital Pharmacy; R. L. McCabe, Michigan Board of Pharmacy; E. R. Jones, Scientific Pharmacy; Miss Cassie Kosiba, Women in Pharmacy; J. L. Powers, University of Michigan; Ernest Crandall, Wayne University; Richard S. Warner, Detroit Institute of Technology, the professors of the respective colleges; and Mr. John H. Webster, Retail Pharmacy.

Mr. H. A. K. Whitney, with 98%, led the contestants and received first award. Mr. Webster struggled in last owing to the fact that he was most unfortunate in picking his questions. However, all the contestants were awarded prizes for their splendid effort and coöperation in making the "Pharmaceutical Quiz" a huge success as well as interesting and highly educational. The judges were Dean R. T. Lakey, chairman of the Program Committee, and Secretary, B. A. Bialk. From the audience Mr. W. H. Blome and Ben Bavly were awarded prizes for answering questions missed by the contestants.

Under new business Mr. Seltzer moved that a letter similar to the one sent to the late Governor Fitzgerald be sent to Governor Dickinson expressing the opinion of the Branch which endorsed a principle in the selection of the members to the Michigan Board of Pharmacy. The motion was seconded by Dean Lakey and carried unanimously. President Smith appointed Dean R. T. Lakey, Leonard A. Seltzer and B. A. Bialk to draw up a suitable letter.

Professor C. H. Stocking of the College of Pharmacy, University of Michigan, announced the tentative program for the Pharmaceutical Conference to be held in Ann Arbor in conjunction with the May 16th meeting of the Branch, at Michigan Union Building, Ann Arbor, Mich. The following papers will be read:

"Some Present Pharmaceutical Problems; Socialized Pharmacy and Working Conditions in Retail Pharmacy," Wortley F. Rudd, Dean, School of Pharmacy, Medical College of Virginia.

"Methods for Evaluation of Antiseptics," Malcolm H. Soule, Professor of Bacteriology and Chairman of the Hygienic Laboratory of the University of Michigan Medical School.

"The Introduction and Development of Antiseptics," F. Blicke, Professor of Pharmaceutical Chemistry, University of Michigan.

"The Pathology of Syphilis as a Public Health Problem," Carl V. Weller, Professor of Pathology and Chairman of the Department of Pathology, University of Michigan Medical School.

Mr. Seltzer moved a rising vote of thanks to Secretary Bialk and Walter M. Chase for the interesting program arranged which provided entertainment, education, fun and prizes for the members of the Branch. The motion was seconded by R. L. McCabe.

BERNARD A. BIALK, *Secretary.*

NEW YORK.—The regular meeting was called to order at 8:45 P.M. on Monday, April 10th, at Columbia University College of Pharmacy. President Canis presided and the meeting was attended by about one hundred members and guests. Minutes of the March meeting were approved.

The Treasurer's report showed a balance of $395.04. Mr. Robert S. Lehman reported for the Committee on Education and Legislation.

A letter from Mr. Edward Gerstenzang pointed out that the first knowledge most retailers have of the N. F. Supplement is on reading them in the Trade Journals. It was moved, seconded and carried that the letter be forwarded to Secretary Kelly with the recommendation by the Branch that revisions of the N. F. monographs be published in the JOURNAL OF THE ASSOCIATION as early as possible.

A second communication from Mr. Gerstenzang objecting to a recent cover published by

the Saturday Evening Post was discussed at a meeting of the Executive Committee held earlier in the evening and the matter referred to the New York Pharmaceutical Council without recommendation.

There being no further business the meeting turned to the Scientific Section. Mr. Gustave Bardfeld acted as chairman and introduced Dr. Eugene R. Marzullo, Assistant Clinical Professor at the Long Island College of Medicine, who addressed the meeting on "The Anemias And Their Treatment," and Dr. J. A. Curran, Dean, Long Island College of Medicine, who spoke on "The Coöperation Of The Medical Colleges With Pharmaceutical Manufacturers In Research In Medicine." After much discussion, a rising vote of thanks was accorded the speakers.

Exhibits were displayed by Eli Lilly & Co., Abbott Laboratories, E. R. Squibb & Sons and Upjohn Co.

HORACE T. E. GIVENS, *Secretary*.

NORTHERN NEW JERSEY.—The Branch met at Rutgers College of Pharmacy on March 20th, 1939. Dr. M. F. Shaffer, of the Squibb Biological Laboratories spoke on "Some Recent Work on Filterable Virus Agents and Their Relation to Disease." He described the methods used in proving the presence of and identification of the virus. He very interestingly described several virus-caused epidemics of men and other animals. Methods of growing and attenuating viruses for the production of vaccines and the chick embryo method for the production of small-pox vaccine were described.

At the February meeting Dr. Hans Molitor of the Merck Research Laboratories spoke on the "Experimental Data on Sulfanalid Derivatives." He compared the reactions of sulfapyridine with sulfanalid especially in connection with the treatment of pneumonia. Following the talk several very interesting discussions were entered into by the floor. Dr. Wm. Nyiri spoke very favorably of his clinical experiences with sulfapyridine in treating pneumonia patients.

C. L. COX, *Secretary*

PHILADELPHIA.—The April meeting was called to order at 8:00 P.M., on Tuesday, April 11th, at Sharp & Dohme Laboratories, Glenolden, Pa. The minutes of the March meeting were read and approved.

A motion was made by Mr. Simpson, seconded by Professor Cook and duly carried by the body authorizing the officers to transfer the checking account from the Germantown Trust Co. to the Integrity Trust Co. and to use the same.

Professor Nichols, chairman of the Program Committee, announced that a symposium on the new Food, Drug and Cosmetic Act would be the feature of the May meeting, and that Drs. Vanderkleed, Munch and Harrison would each explain some particular phase.

Dr. Osol requested that the members make a special effort to increase our membership during the coming year. The Secretary explained the privileges of full and associate membership.

Dr. John Reichel, Technical Director of the Glenolden Laboratories of Sharp & Dohme, was introduced by the chairman. He gave a very interesting and informative talk on lyophile substances and the lyophile process. He explained that biologicals were very sensitive protein substances, and the difficulty experienced in preserving them with chemicals or ordinary cold storage. Lyophile substances are materials that are rapidly frozen, then rapidly dehydrated under high vacuum while still in the frozen state. Preparations so processed are porous, bulky, rapidly soluble and remarkably stable. After explaining in detail the theory and technique of manufacture, slides were shown portraying the development of the process. Various products made in this manner were then displayed. Dr. Reichel answered the many queries of the members. He was then accorded a rising vote of appreciation.

Dr. Osol expressed the thanks of the organization to Mr. Miller for his hospitality and that of Sharp & Dohme for the dinner they so generously tendered us.

R. H. BLYTHE, *Secretary*

TEMPLE UNIVERSITY STUDENT BRANCH.—On January 16th, the chapter formally applied for a charter and forwarded dues and applications for 16 members. February 21st, a special meeting was held for the election of officers. Those elected were Donald Johnson, *President;* Irvin Lipman, *Vice-President;* Reba Nevel, *Secretary;* and Alton Grube, *Treasurer*. The president soon thereafter appointed the *Program Committee*, consisting of M. Krigelman,

Chairman; Irvin Lipman and Alton Grube; the *Membership Committee*, Grellanda Eannaccone, Eugene Reese, Rose Parker, and William Wittmer.

On February 23rd, the entire student body participated in a convocation at which the officers of the Student Branch were inducted by Dr. Ernest Little, dean of the School of Pharmacy of Rutgers University and chairman of the Committee on Local and Student Branches. The Charter was presented to the chapter by Dr. Leon Lascoff, president of the A. PH. A., and one of America's distinguished pharmacists.

On February 28th, the School of Pharmacy had as visitors, Dr. E. F. Kelly, secretary of the A. PH. A. and Dr. H. C. Christensen, secretary of the National Association of Boards of Pharmacy. Dr. Kelly spoke of the value of organization. He also emphasized the importance of the AMERICAN PHARMACEUTICAL ASSOCIATION to students and the importance of students to the organization.

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The meeting was called to order Tuesday evening, April 17th, in the club room of Mitten Hall by the President, Donald Johnson. A summary of previous activities was read and approved.

A motion was made and carried that the new branch keep a permanent file of clippings pertaining to its activities. Miss Steigerwald was appointed chairman of this committee, and all members of the branch will assist her in collecting this material.

Miss Drozd, '39, read a paper on "Leprosy." She gave some interesting data on the history of the disease, then emphasized the sanitary conditions and excellent care given the lepers in their colonies. Dr. Cobe, assistant professor of Bacteriology and Public Health, took over with an informal talk on the same subject. He added interesting information of the bacteriological theories on the source of infection, communicability and incubation period. There followed a round-table discussion during which Dr. Cobe answered questions and related his experiences with the disease. Thanks were extended to the participants.

Dr. Eby, professor of Pharmacognosy and faculty advisor to the Branch, discussed the value of the A. PH. A. JOURNAL to the student. He suggested a close surveillance of the scientific abstracts included in the JOURNAL as a means of keeping abreast of modern scientific developments. He further suggested, relative to those abstracts, as yet unintelligible to the student, a ready cross-index file of current abstracts for future reference.

For the next meeting, May 16th, members will invite guests.

REBA NEVEL, *Secretary*

UNIVERSITY OF MISSISSIPPI STUDENT BRANCH.—The first meeting was held on December 8, 1939, at the Pharmacy building. It was called to order by the President, Verdell Yelverton. An election of officers for the year was held with the following results: *President*, Freeman C. Hays; *Vice-President*, Lucille Sullivan; *Secretary*, Marguerite Holmes; *Treasurer*, Wayne Logan; *Reporter*, Harriet Walker. Dean E. L. Hammond was elected *Faculty Advisor* by acclamation. Committees were appointed by the new president. It was decided that all members should serve on the membership committee and a membership drive be started. It was also agreed that the rebate from last years dues be used for a page in *Ole Miss* annual.

On February 14th an informal meeting was held in the dining room of the University Cafeteria, in the form of a banquet. Dean E. L. Hammond introduced Henry M. Faser, former dean of the Pharmacy School, who made a short talk. The speaker for the evening, Robert P. Walton, was then presented. Dr. Walton, professor of Pharmacology, gave a very interesting discussion on marijuana, a subject on which he has recently done research.

Marguerite Holmes, *Secretary.*

THE SEVENTEENTH ANNUAL PLANT SCIENCE SEMINAR.

On August 14th to 19th the Plant Science Seminar will meet at Blue Ridge College, Blue Ridge, N. C., fifteen miles east of Asheville. Room rates vary from $1.00 without bath to as high as $2.50 with bath. Meals can be had in a splendid cafeteria for as low as $1.00 a day; or, if you wish, best hotel service at $2.00 per day. A delightful program has been arranged, with many natural attractions. The distance to Atlanta is 250 miles, where the AMERICAN PHARMACEUTICAL ASSOCIATION will assemble in convention the following week. Trips to the historic city of Charleston, or to Chapel Hill, site of the University of North Carolina, can be arranged.

Details of Program will appear later.

PERSONAL AND NEWS ITEMS.

M. Demarais, pharmacist and municipal councillor, Honfleur, France, was among several aspirants to the Presidency of his country. However, he later withdrew from the contest. Monsieur Demarais is the proud possessor of numerous honors and medals.

Dr. W. H. Morehouse, president of Drake University, has announced the merger of Des Moines College of Pharmacy with the university. The Pharmacy School becomes the College of Pharmacy of Drake University; and the student body, equipment and faculty will be moved to Drake Campus. The College will be housed in Science Hall which is now undergoing remodeling. Dean E. O. Kagy will continue as dean of the Pharmacy School.

For the second successive year, M. Rene Tanquery, Consul General of France in New York, on behalf of his government, has presented to the French Department of Fordham College two silver medals and three bronze medals to be presented to the students showing the greatest proficiency in French. The awards were made at the suggestion of the French Minister of Foreign Affairs.

The Seventh Annual Science Day exhibits will be presented by the Philadelphia College of Pharmacy and Science on April 21st and 22nd, 1939.

The American Association of Museums will meet in San Francisco June 26th to 28th. Hotel St. Francis will be headquarters. The Golden Gate Exposition will be in full swing at that time.

The Ohio Hospital Association met in Columbus, O., April 11th to 13th. Dean Edward Spease made an address an "The Hospital Pharmacy of the Future." Hospital pharmacists from all over the state attended. Roger Lager, chief pharmacist at University Hospitals, Cleveland, was elected *President;* and Stanley Dorsey, chief pharmacist at Holmes Hospital, Cincinnati, *Secretary.* It is expected that great benefits will be the result of an exchange of ideas, technique, etc.

About seventy retail druggists of Philadelphia, Pa., including members of their families, enjoyed a trip to Washington and visited the American Institute of Pharmacy on Sunday, April 16th. Dr. S. L. Hilton welcomed the party and the visitors were shown through the building.

Among recent visitors at the American Institute of Pharmacy were: Mr. W. P. Porterfield of Fargo, North Dakota, member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1909; and Prof. Alexander Stewart of Guelph, Canada, with members of his family and friends.

The Oklahoma Pharmaceutical Association met in Oklahoma City, April 18th to 20th. A number of interesting and well-known speakers were on the program, among them: F. L. Unzlicker, "Distributive Education;" Ralph A. Beegle, "Emphasizing the Profession;" Robert L. Swain, "Caucus, Congressional Districts;" L. E. Harris, "The Federal Pure Food, Drug and Cosmetic Act, As It Applies to you;" Nevelle McKinney, a Senior at the Oklahoma School of Pharmacy, read a paper on, "Better Employer and Employee Relations." The year just closing has been a busy one for the Association with a fine record of accomplishment.

The Nebraska Pharmaceutical Association met in Lincoln on April 17th to 20th. An unusually fine Drug Show was arranged. President Gulley called the convention to order and delivered his address, which was an interesting report of the year's work. Among the speakers were: Otto Kuether, "National Pharmacy Week;" Ed Gannon, "Modernization of Our Drug Stores," Dr. Neal Bowman, Temple University, Philadelphia, Pa., "Impressions Build Prescription Business;" B. R. Mull, "Professional Relations."

Mr. John E. O'Brien, of Omaha, Nebr., was appointed by Dr. J. Leon Lascoff, president of the A. PH. A., as chairman of the 1939 Pharmacy Week Committee.

The Missouri Pharmaceutical Association met in St. Louis, May 8th to 11th. The chief subject of discussion was, "10,000 Helps in Selling and Practical Display Work." A number of speakers of National prominence appeared on the program. An interesting feature of the convention was a Drug Show. Druggists in St. Louis have been busily engaged in working for the adoption of the Fair Trade law.

The Kansas Pharmaceutical Association met in Wichita on March 20th to 23rd, with more than 800 registered. Among the speakers were: Ralph A. Beegle, "Merchandising;" Leon R. Kramer, "Our Health Program;" J. W. Snowden, "Dramatization of the Prescription Department;" Tom Gouchman, "Get Yourself a Partner." W. S. Daugherty, of Syracuse, was elected president; the youngest man ever to have been so honored.

The Illinois Pharmaceutical Association met in Peoria May 16th to 18th. Among the many interesting addresses heard was one by J. J. Donlan of *The American Weekly*, on "Dollars—Not Percentages—Meet the Pay Roll and Pay the Rent." In addition to the regular business sessions there were reports of the past year's work, an account of the progress on the new Pharmacy Law, facts on the continued growth of the Fair Trade movement in the state and an opportunity for every one to express his opinions on the policies of the Association.

The Iowa State Pharmaceutical Association held its 60th convention in Des Moines recently. Emphasis was placed on professional pharmacy legislation, and the major resolution was "to concern ourselves, at present, with only professional pharmacy legislation, excluding all other types of legislation, including commercial." Among the speakers were: Dean C. H. Rogers, Minnesota College of Pharmacy; J. W. Snowden, Pictorial Paper Package Corporation; Elmer A. Gissell, Mt. Pleasant Hospital pharmacist. Merchandising problems were discussed by: Joseph J. Shine, secretary Illinois Pharmaceutical Association; DeLoss Walker, associate editor of *Liberty Magazine;* I. H. Bander, vice-president of McKesson & Robbins, New York City. Hugh Tyler, of Lenox, discussed "Should We Make the Drug Store the Sole Outlet for Insecticides and Denatured Alcohol?"

Dr. Hugo H. Schaefer, dean of the Brooklyn College of Pharmacy, explained how retail druggists are affected by the new Federal Food, Drug and Cosmetic Act at the convention of the New York Pharmaceutical Council on April 25th and 26th, Hotel Pennsylvania. Other speakers were: Samuel S. Dworkin, chairman, Council's Trade Committee; John W. Dargavel, secretary of the N. A. R. D.; Nathan Zonies, president of the Pennsylvania State Pharmaceutical Association; Harry H. Miller, director of the N. Y. State Pharmaceutical Association's Fair Trade Committee; John S. Norton, vice-president of the Lambert Pharmacal Co.; and John C. Davis, president of the N. W. D. A.

After forty years as teacher and nurse, **Sister Mary McLaughlin** of St. Mary's Hospital, Grand Rapids, Mich., felt the desire to better serve the hospital. She therefore entered Ferris Institute and a year later became a registered pharmacist. Recently she celebrated her fiftieth anniversary as a member of the Sisters of Mercy.

Mr. George A. Moulton addressed the meeting of District No. 1, A. A. C. P. and N. A. B. P., in Boston recently, on "Socialized Medicine."

Assuming that the socialization of medicine is certain to involve basic pharmaceutical interests, the Wisconsin Pharmaceutical Association has undertaken a comprehensive survey of the pharmacist's place in the various health plans now in effect in England and the countries of continental Europe. **Mr. Jennings Murphy,** secretary, is in charge of the work.

Dean A. H. Clark, University of Illinois, College of Pharmacy, spoke on "Journeys in the Far West," at a recent meeting of Phi Chapter of Rho Chi, National Honorary Pharmaceutical Society, when new members were initiated at a banquet at the West Side Professional Schools Y. M. C. A., in April.

Mr. B. Tappen Fairchild, of Fairchild Brothers & Foster, New York City, has been left complete control of the stock under the provisions of the will of his uncle, Benjamin Thomas Fairchild, founder of the company, who died March 25th. Mr. Fairchild also inherits his uncle's four-hundred acre estate in Greenwich, Conn.

Dr. E. Fullerton Cook, chairman of the U. S. P. Revision Committee, sailed on April 21st to attend the annual conference of the Commission of Pharmacopœial Experts of the Health Organization of the League of Nations which opens in Geneva, May 10th. This commission plans to meet each year to establish international standards for medicines used all over the world and to prepare monographs for therapeutic agents offering such monographs to the pharmacopœial committees of the various nations for voluntary adoption.

OBITUARY.

WARREN LANSING BRADT.

Warren L. Bradt, president and treasurer of the Bradt Drug Co., Albany, N. Y., died suddenly on March 4th, at his home. He had been a member of the AMERICAN PHARMACEUTICAL ASSOCIATION since 1911.

Mr. Bradt was secretary of the State Board of Pharmacy 1900–1925 and had been president of Albany College of Pharmacy since 1928. He was active in many civic and fraternal organizations, the Holland Society, Masters' Lodge of Masons, Shrine, Knights Templar and Rotary Club, and was a vestryman at St. Paul's Episcopal Church. He was a member and former vice-president of the Protestant Family Welfare Association.

Funeral services were held on Tuesday afternoon at St. Paul's Episcopal Church with Rev. George A. Taylor officiating; burial was in Oakwood cemetary, Troy.

Besides his widow, Mrs Irene Sitterly Bradt, Mr. Bradt is survived by a sister, Mrs. W. H. A. Hall, and two nieces, Dorothy and Mary Bradt Hall, of Millburn, N. J.

JAMES H. MARSHALL.

James H. Marshall, member of the AMERICAN PHARMACEUTICAL ASSOCIATION, and one of the founders of the Northwestern Drug Co., Minneapolis, died April 13th, aged eighty-three years.

Mr. Marshall served as president of the Federal Wholesale Druggists' Association in 1922 and from 1927–1931. At the time of his death he was honorary president of the Association.

For many years Mr. Marshall was a member of Westminster Church, Minneapolis.

Mrs. Marshall and two daughters, Sara of New York City and Margaret of Winona, Minn., survive.

Funeral services were held at Lakewood Chapel with burial in Lakewood Cemetery, Monday, April 17th.

HENRY PFEIFFER.

Mr. Henry Pfeiffer, president of William R. Warner & Co. New York City, died April 13th, aged eighty-two years. In 1908 Mr. Pfeiffer purchased Wm. R. Warner & Co., then located in Philadelphia; and moved the Pfeiffer Chemical Co. from St. Louis to New York. At the time of his death he was vice-president and director of the Richard Hudnut Co., president of the Bauer Chemical Co., the Vince Laboratories, Inc., the Nonspi Company and the Sanitol Co.; vice-president of the Hudnut Sales Co., and a director of Warner International.

In March 1882 Mr. Pfeiffer married Miss Annie Merner. They celebrated their fifty-seventh wedding anniversary last month. Besides his widow there are five brothers surviving, among them Mr. G. A. Pfeiffer, of New York City, member of the AMERICAN PHARMACEUTICAL ASSOCIATION.

R. E. LEE WILLIAMSON.

Mr. Williamson, member of the AMERICAN PHARMACEUTICAL ASSOCIATION and other associations, manager of the Mutual Drug Co., of Cleveland, and treasurer of the Noxzema Chemical Co., Baltimore, Md., died April 29th, at his home in the Hammond Apartments, Baltimore, Md. He had been in ill health for a year but his condition was not acute until a month ago when he was brought home from a vacation in St. Petersburg, Fla.

At the time of his death he was secretary of the Federal Wholesale Druggists Association. He had served as president of the Baltimore Retail Druggists Association for more than fifteen years, and as president of the Maryland Pharmaceutical Association. He was nationally prominent in drug circles, having been associated with the retail and wholesale drug business for many years.

Funeral services were held on Tuesday, with burial in Loudon Park Cemetery. He is survived by his widow, Mrs. Grace Williamson and a daughter, Mrs. Charles Keller, of Frederick.

BOOK NOTICES AND REVIEWS.

Text Book of Pharmacology, Toxicology and Prescription Writing, by EMIL STARKENSTEIN, M.D., with the coöperation of Prof. Dr. Hedwig Langecker, Dr. Franz Hendrych, Karl Klimersch, M.P. and Dr. Hans Weden. Dr. Starkenstein is a professor of Pharmacology and Pharmacognosy at the German University in Prag. The volume has more than 750 pages, 40 illustrations and is distributed by Franz Deuticke, Leipzig and Wien.

The author refers to a definition by S. Dale in London, 1692, as related to Materia Medica; he named it a description of the medicinal substances and states that this also includes the newer remedies, biologicals and toxicology, conforming to the title of the book. The treatise embodies, in General Pharmacology,

the standardization of the materia medica and the dosage. The General Toxicology is a study of poisons.

Therapeutics as all other subjects, shows a system of treatment of the drug and of the condition for which it is administered and applied. Rules are laid down for the physician for prescribing application and action. Anesthetics, narcotics, sedatives, hypnotics are comprehensively studied individually, in groups, in combinations, dosage, etc. Another division includes the heart, the blood, circulation, glands, vitamins, hormones; the lungs and other organs receive systematic consideration.

Therapeutics, as all other subjects, shows a system of treatment of the drug and of the condition for which it is administered and applied. A criticism of the work might be that the effort is too comprehensive, a review prepared accordingly would require lengthier discussion than it is possible to give, and the author is favorably known to those who will use the volume.

The Plant Alkaloids, by THOMAS ANDERSON HENRY, director, Wellcome Chemical Research Laboratories. Third Edition. Published by P. Blakiston's Son & Co., Inc., 1012 Walnut St., Philadelphia, Pa. 689 pages; washable fabric; price, $12.00.

Much new information has accumulated concerning plant alkaloids since the publication of the second edition. The third edition has involved rewriting the volume and adding considerable to its bulk. The material available has been compiled primarily on the basis of chemical classification according to nuclear structure. This primary classification has been modified in a biological direction wherever necessary. Where this has resulted in some groupings being dealt with in more than one place, cross-references have been provided to obviate any inconvenience due to this departure from a rigid system. The author has kept in view the various aspects of the subject and the articles on all of the more important alkaloids describe the properties, chemistry, occurrence, methods of estimating and physiological action.

The table of contents consists of the following: Pyridine Group—Piperidine and Acylpiperidines, Alkaloids of Ricinus communis, Foenugree, Areca Nut, Hemlock, Lobelia, Tobacco, Anabasis aphylla and Pomegranate Root Bark; Tropane Group—Solanaceous Alkaloids, Alkaloids of Dioscorea hirsuta, Coca Leaves (Erythroxylon coca); Lupinane Group—Alkaloids of the Papilionaceæ: Lupinine, Lupanine, Sparteine, Anagyrine, Cytisine, Matrine and the Associated Bases; iso-Quinoline Group—Alkaloids of: Cactaceæ Mezcaline, Anhalamine, etc.) Hydrastine, Papaveraceæ (botanical distribution), Opium (benzylisoquinolines; Morphine Sub-group, including Sinomenium Bases), Other Papaver spp. (Rhoeadine, Aporeine, etc.), Other Papaveraceous genera (α-Homochelidonine, Chelerythrine, Chelidonine, Sanguinarine, etc.), Corydalis and allied genera (Tetrahydroprotoberberines; Cryptopine Sub-group; Aporphine Sub-group: Phthalideisoquinolines), Lauraceæ and Monimiaceæ (Laurotetanine, Actinodaphnine, Pukateine, Laureline, etc.), Ipecacuanha (Emetine, Cephæline, etc.), Berberis spp. (Berberine, Canadine, Berbamine, Oxyacanthine, etc.), Menispermaceæ (Coclaurine, Dauricine, Trilobine, Menisarine, Berberine, iso-Chondrodendrine, etc.), Curare (Curine, Tubocurarine, Protocuridine, Neoprotocuridine, Calabashcurarine); Phenanthridine Group—Alkaloids of Amaryllidaceæ (Lycorine, Sekisanine, Tazettine and the Allied Bases); Quinoline Group—Alkaloids of Echinops, Dictamnus and Skimmia spp., Cusparia Bark (Cusparine, Galipine, etc.), Cinchona spp. Quinine, Quinidine, Cinchonidine, Cinchonine, etc.); Indole Group—Alkaloids of Abrus, Erythrina, Arundo, Calycanthus spp., Peganum Harmala (Harmaline, Harmine), Evodia rutaecarpa (Evodiamine, Rutæcarpine), Yohimbe' and Quebracho (Yohimbine, Corynanthine, Corynantheine, etc.), Ergot (Ergotoxine, Ergotamine, Ergometrine, etc.), Calabar Bean (Physostigmine, etc.), Strychnos spp. (Strychnine, Brucine and the Allied Bases); Pyrrolidine Group—Carpaine; Quinazoline Group—Vasicine (Peganine); Glyoxaline Group—Alkaloids of Pilocarpus spp.; Alkaloidal Amines—Damascenine, Hordenine, Alkaloids of Ephedra spp., Brassica spp., Cheiranthus and Erysimum spp., Colchicum antumnale, Amanita muscaria; Alkaloids of Undetermined Constitution; Minor Alkaloids.

In most cases the original memoirs have been consulted and references to these are given in the footnotes. For description of the physiological action of the better-known alkaloids Cushny's "Textbook of Pharmacology and Therapeutics," has been largely utilized. The chemical nomenclature and system of abbreviations are those of the book as well as several important tables.—EMERSON C. BEELER.

PROGRAM FOR THE ATLANTA MEETING.

It is intended to publish the entire General Program in the July issue of the JOURNAL. It will therefore be greatly appreciated if the secretary of the Sections, AMERICAN PHARMACEUTICAL ASSOCIATION, of the American Association of Colleges of Pharmacy, the National Association Boards of Pharmacy, the Conference of Pharmaceutical Association Secretaries, Conference of Pharmaceutical Law Enforcement Officials, National Conference of Pharmaceutical Research and the Plant Science Seminar will mail their copy to the JOURNAL office at the earliest possible date in order that manuscript may be put in shape for the printers and set in type so as to have the July JOURNAL in the mails on time.

PREPARATION OF PAPERS.

All manuscripts should be typewritten in double spacing on one side of paper $8^1/_2$ x 11 inches, and should be mailed in a flat package—not rolled, to the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 2215 Constitution Ave., Washington, D. C. Papers to be submitted at the annual meeting should be forwarded to the Secretary of the appropriate Section. The original and one copy must be sent together with an abstract of not more than 250 words. The abstract should include a summarization of the conclusions and recommendations, if any, reached by the author or authors of the paper. The original drawings, not photographs of drawings, should accompany the manuscript. Authors should indicate on the manuscript the approximate position of text figures. All drawings should be marked with the author's name and address.

A condensed title running page headline, not to exceed thirty-five letters, should be given on a separate sheet and placed at the beginning of each article.

The method of stating the laboratory or other place in which the work is done should be uniform and placed as a footnote at end of first page, giving Department, School or College, etc. The date when received for publication should be given.

Numerals are used for figures for all definite weights, measurements, percentages and degrees of temperature (for example: 2 Kg., 1 inch, 20.5 cc., 300° C.). Spell out all indefinite and approximate periods of time and other numerals which are used in a general manner (for example: one hundred years ago, about two and one-half hours, seven times).

Standard abbreviations should be used whenever weights and measures are given in the metric system, *e. g.*, 10 Kg., 2.25 cc., etc. The forms to be used are: cc., Kg., mg., mm., L. and M.

Figures should be numbered from 1 up, beginning with the text-figures (line engravings are always treated as text-figures and should be designed as such) and continuing through the plates. The reduction desired should be clearly indicated on the margin of the drawing. All drawings should be made with India ink, preferably on white tracing paper or cloth. If coördinate paper is used, a blue-lined paper must be chosen. Usually it is desirable to ink in the large squares so that the curves can be more easily read. Lettering should be plain and large enough to reproduce well when the drawing is reduced to the width of a printed page (usually about 4 inches). Photographs intended for half-tone reproduction should be securely mounted with colorless paste.

"Figure" should be spelled out at the beginning of a sentence; elsewhere it is abbreviated to "Fig.;" per cent—2 words.

The expense of figures and plates, not exceeding three, will be borne by the JOURNAL; expense for cuts in excess of this number must be defrayed by the author.

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(1) Author, A. Y., *Am. J. Physiol.*, 79, 289 (1927).

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